Investigation and Management of Bone Mineral Density Following Hematopoietic Cell Transplantation : A Survey of Current Practice by the Transplant Complications Working Party of the European Society for Blood and Marrow Transplantation

Salooja, Nina

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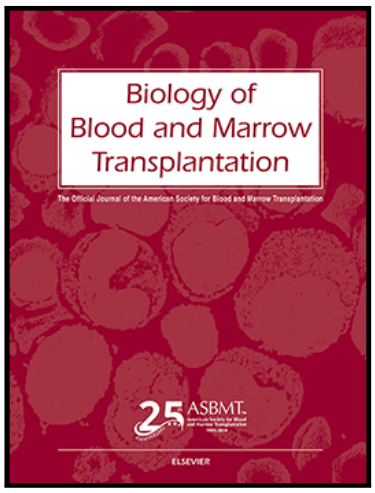

Investigation and management of bone mineral density following HCT: a survey of current practice by the Transplant Complications Working party of the European Society for Blood and Marrow Transplantation

N Salooja , H Greinix , T Ruutu , SM van der Werf , A van Biezen , A. Lawitschka , G. Basak , R Duarte

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Highlights

- Low bone mineral density is frequent after haematopoietic cell transplantation
- There is inconsistency of practise in relation to guidelines on BMD after HCT
- There was a lack of familiarity with BMD guidelines among centres for HCT in Europe

TITLE PAGE

Investigation and management of bone mineral density following HCT: a survey of current practice by the Transplant Complications Working party of the European Society for Blood and Marrow Transplantation.

N Salooja, H Greinix, T Ruutu, SM van der Werf, A van Biezen, A. Lawitschka, G. Basak, R Duarte

Corresponding author:
Dr Nina Salooja
Mobile number : 0044 7831621067
Secretary's number: 0044 2083838117
Email: nina.salooja@ic.ac.uk

NAME	AFFILIATION
N Salooja	Centre for haematology, Hammersmith Hospital, Imperial College London, London, UK
H Greinix	Department of Internal Medicine, Medical University of Vienna, Vienna, Austria
T Ruutu	Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland
SM van der Werf	Department of Medical statistics and bioinformatics, Leiden, The Netherlands
A van Biezen	Department of Medical statistics and bioinformatics, Leiden, The Netherlands
A Lawitschka	St. Anna Children's Hospital, Medical University of Vienna, Vienna, Austria
G Basak	Department of Haematology, Oncology and Internal diseases Medical University of Warsaw, Warsaw, Poland
R Duarte	Department of Hematology, University hospital Puerta de Hierro, Madrid, Spain

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Abstract

Reduced bone mineral density (BMD) is a well recognised complication of haematopoietic cell transplantation (HCT) with significant falls in BMD occurring within the first 12 months of HCT. Guidance on identifying and managing this complication is available in several published guidelines. In this study we have sought to investigate current practise in the investigation and management of low BMD in centres registered with the European Society for Blood and Marrow Transplantation (EBMT). A questionnaire about bone health was sent to all registered centres and responses gained from 99 centres in 25 (52%) countries currently registered with the EBMT. Our data highlights considerable heterogeneity of practise across European centres in relation to investigations, management and use of guidelines. Our data highlights the need for better dissemination and implementation of existing guidelines but also for the development of multidisciplinary guidelines with input from all relevant stakeholders.

Key words: Bone mineral density, haematopoietic cell transplantation, survey of practice

Investigation and management of bone mineral density following HCT: a survey of current practice by the Transplant Complications Working Party of the European Society for Blood and Marrow Transplantation.

Introduction

Reduced bone mineral density (BMD) is a well recognised complication of haematopoietic cell transplantation (HCT). The prevalence of low BMD after allogeneic HCT is variably quoted as 24-48% (1-3) and is higher in patients with chronic graft-versus-host disease (GVHD) (4). Studies demonstrate that a fall in BMD occurs within the first 12 months of transplant and is particularly rapid in the first 6 months (5-6). A similar pattern of bone loss has also been described after autologous transplantation (5). Typically this reduction in BMD is followed by some recovery in the lumbar spine with slower improvement at the femoral neck (7,8). The mechanisms underpinning bone loss after HCT are multifactorial and are associated with both a decrease in osteoblast activity (bone formation) and an increase in osteoclast activity (bone resorption). Dysregulation of cytokines from the TNF superfamily are associated with this imbalance, in particular receptor activator of nuclear factor kappa-B (RANK) ligand and osteoprotegerin (OPG) (9,10).

Clinically the main concern with a reduction in BMD is the potentially increased risk of fracture which approximately doubles for each standard deviation decrease in BMD (11,12). In general populations osteoporotic fractures are associated not only with pain and disability, but also with a significant increase in mortality (13,14).

Bone mineral density is measured by Dual-energy X-ray absorptiometry (DXA) scanning and this can be used to diagnose osteoporosis or osteopenia in adults. Measurements in the lumbar spine, or femoral neck and/or hip are compared with the mean BMD of a normal young adult population of the same gender to give a T-score. A T-score of < - 2.5 in any site indicates osteoporosis and a T-score between -1 and -2.5 designates osteopenia. While there is a clear link in adults between DXA scan data at these sites and both risk of fracture and response to treatment (15), in children these links are less clear. DXA scanning cannot account for bone size or shape and can underestimate BMD in children where the bone size is low. Quantitative computed tomography (QCT) scanning may be more accurate than DXA scanning in paediatric patients (16). Where the latter is used, however, Z scores are preferable in paediatric populations to T scores because they are age, sex and gender matched. Measurements are taken at the lumbar spine or else as total body readings (which exclude the head). In children, the term osteoporosis is reserved for those with a low Z score (<-2) combined with a clinically significant fracture history.

Low BMD measured by DXA is not the only risk factor for fracture in the general population. The World Health Organization Fracture Risk Assessment Tool (FRAX) takes into account multiple factors to estimate 10-year probability of major fracture in patients aged 40-69 (17). Risk factors additional to age include low body mass index (BMI), prior fracture, family history of fracture, smoking, alcohol, use of glucocorticoids (GC) and rheumatoid arthritis. Although validated in non-transplant settings (18-20), experience using the FRAX model in HCT recipients is limited: a single centre retrospective study demonstrated modest predictive value in patients older than 50y but further validation in specific populations would be necessary before it could be recommended for routine use (21). Transplant patients have additional risk factors for fracture compared to the general population including chemotoxicity, radiation, secondary hyperparathyroidism and hypogonadism. Underlying disease is also important with diagnoses of acute lymphoblastic leukemia and multiple myeloma conferring additional risks of bone fracture (22,23). Age is likely to be increasingly relevant as more and more older patients are included in transplant programmes.

A fall in bone density in relation to HCT is frequent and data indicates that it can potentially be mitigated and treated (24). Attention to bone health has therefore been included in several long term post- transplant follow up guidelines for adults and children within the last 15 years (25-30). In this survey we have investigated the current practise in assessing and managing bone health in centres registered with the EBMT.

Materials and methods

453 transplant centres from 48 countries were invited to participate in an on-line survey. These included both adult centres (defined as >70% patients are adults) and paediatric centres (defined as >70% patients are paediatric). The survey was open for approximately 12 months and closed in January 2018. The survey included 10 questions relating to counselling patients about bone health, indications for DXA scanning before or after transplant, timing of DXA scanning, management of reduced bone mineral density (osteopenia and osteoporosis), use of prophylactic treatment for reduced BMD, trigger doses of GC for DXA scanning and use of guidelines. In 2020 a follow up question asked

whether national policy/insurance restrictions played a significant part in the decision making around frequency and timing of DXA scanning or in the choice of drug used to treat osteopenia/osteoporosis.

Results

A total of 99 centres from 25 countries participated (figure 1). This represented a 22% response rate overall with data included from 52% of the countries currently registered with the EBMT. From eight countries there were responses from 5 or more participating centres (France, Germany, Italy, Netherlands, Spain, Sweden, Turkey and the UK). Twelve of the 99 responding centres were designated paediatric and within these the percentage of adults being treated was low with 4/12 centres not treating any adults and the remaining 8 centres treating a median of 4% adults (range 1-6%). Response rates for each question varied and are indicated by the denominators in the text.

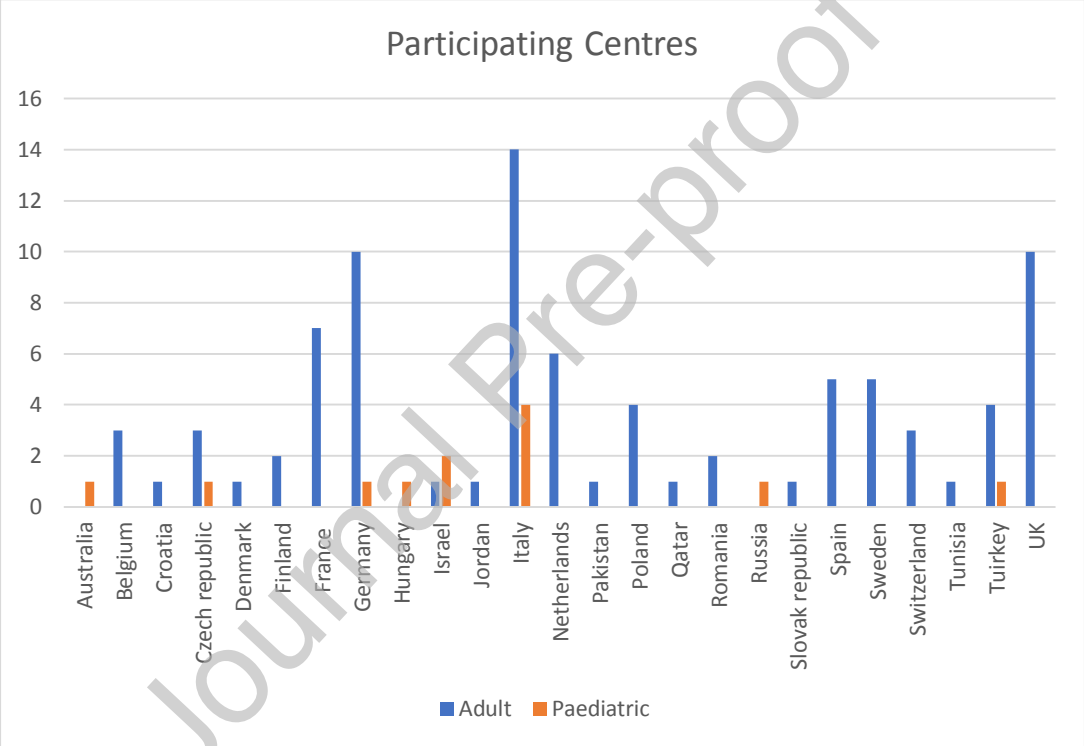

Figure 1. The number of adult and paediatric centres responding from each participating country

Patient guidance on maintaining/Improving bone health after HCT

Of 92 respondents to this question (10 paediatric), 73 (79%) centres (8 paediatric) indicated that they gave guidance to their patients about lifestyle measures for promoting bone health after HCT. Among these centres guidance was solely verbal in 41/73, written-only in 5/73 and both verbal and written in 27/73. The most frequent advice was dietary, promoting an increase of vitamin D (26/73) or calcium (18/73). Other elements of lifestyle advice included the value of exercise (20/73) and smoking cessation (6/73).

Indications for DXA scanning

47/99 (47%) centres did not have routine triggers for conducting DXA scanning. Of the 52 centres that did, 37 based their approach on the type of transplant, age or sex of the patients. More specifically 11 centres scanned all patients after HCT (allograft, autograft, myeloablative, reduced intensity), 20 centres scanned all allograft patients after HCT, one centre scanned everyone over the age of 60 and another scanned all allografts over the age of 60. Four centres scanned all females over 60.

Among 11 centres which conducted DXA scanning on all patients after HCT, three of them also conducted DXA scanning on all patients before HCT. One additional centre undertook pre transplant DXA scanning only if the patient had a family history of osteoporosis or else had received GC pre transplant.

Among 20 centres which scanned all allograft recipients after HCT, 11 also arranged DXA scanning for all allografts before transplant. One additional centre arranged pre-transplant DXA scanning if the patient was being allografted over the age of 60 or else had received pre transplant GC.

Fifteen centres used specific risk factors for low bone mineral density (BMD) as triggers for DXA scanning. Amongst these 15 centres, the median number of risk factors cited per centre was 3 but the range was wide at 1-8. An additional 26 centres who restricted DXA scanning on the basis of transplant type +/- gender +/- age, also considered risk factors for low BMD in their protocols. The most frequent risk factors considered were use of GC after transplant (n=25) and vitamin D deficiency (n=14). Other risk factors considered by participating centres are summarised in figure 2.

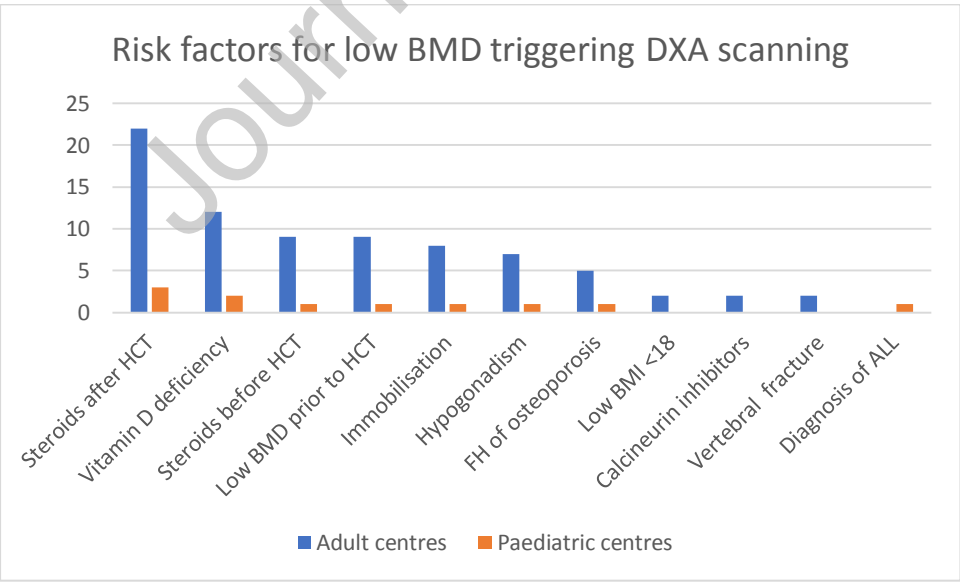

Figure 2: Risk factors for low BMD which trigger DXA scanning after HCT

Abbreviations: FH = family history; BMI = body mass index; ALL= acute lymphoblastic leukemia.

12/99 responding centres were designated paediatric centres. 3/12 screened all transplant patients post transplant and of these one also undertook screening of all patients before while another centre undertook tailored screening before transplant if a patient had received GC or else had a FH of osteoporosis. 1/12 paediatric centres screened all allograft recipients post transplant. In two paediatric centres, screening was based on individual risks. The remaining 6 paediatric centres did not conduct routine DXA scans.

Timing of routine DXA scanning after HCT

49/52 centres who perform regular scans responded to this question. The most frequent time point for a first routine DXA scan was 12 months, but there was some variability in both adult and paediatric centres (figure 3). Fifteen of these 49 centres arranged routine scans at more than one time point, with 11 /15 arranging DXA at two time points and 4/15 scheduling three or more. The most frequent patterns were: 1. 0-6 months or 6-12 months followed by another at 12 months (n=6) 2. 12 months or 12-24 months followed by another at 2-5 years (n=4).

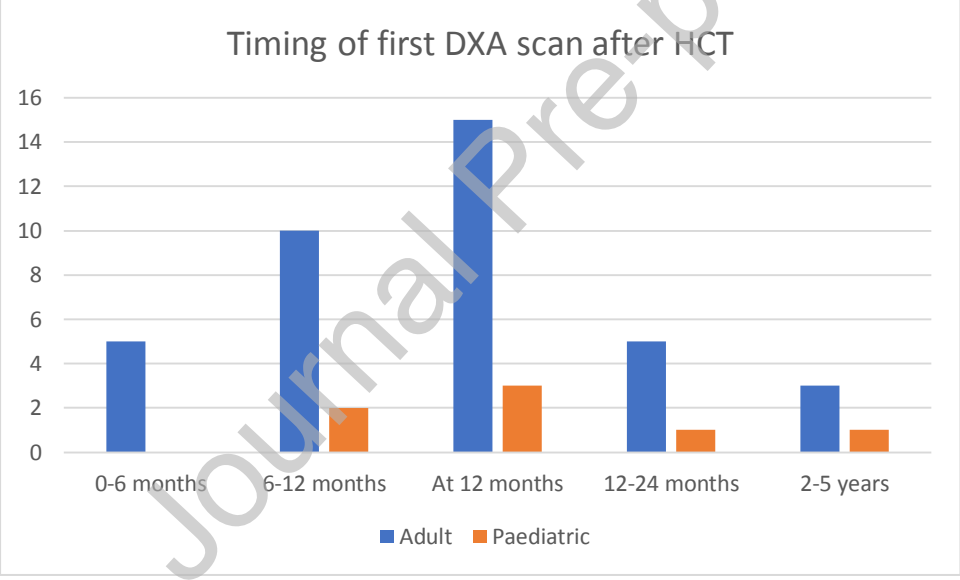

Figure 3: Timing of first scheduled DXA scan after HCT

Time interval between scans

Where a patient was diagnosed with osteoporosis, 75 /90 respondents indicated that they would do a follow up scan. The median time interval was 12 months (34 respondents) with more than half of these centres indicating that they would continue to repeat the scans annually. In 8 cases the centre indicated that the decision would be made by a non-haematology specialist.

Where a patient was diagnosed with osteopenia, 68/89 respondents indicated that they would do a follow up scan. Again the median time interval was 12 months (31 respondents) with 16 of these indicating that scans would be requested annually. In 5 centres the decision was made by non-haematology specialists.

A single centre reported that insurance schemes dictated the frequency of DXA scanning when a diagnosis of osteoporosis or osteopenia had been made.

Steroid dose/duration triggers for DXA scanning

Thirty centres specified that GC after and /or before HCT were a trigger for DXA scanning. The cut-off doses/duration of treatment for measuring bone density were given in 27/30 and were variable. In 7 centres, duration of treatment only was a consideration with 5 time points cited: 'prolonged' dosing (n=1), > 1 month (n=1), > 2 months (n=1), 3 months (n=1), > 3months (n=3). The remaining 20 responding centres cited 14 different schedules involving both dose and duration (Table 1). Paediatric centres which used post +/- pre transplant GC as a trigger for DXA scanning specified 3 different regimens that would trigger DXA scanning as follows: 1mg/kg for 6 months, > 1mg/kg for 6 months and 2mg/kg/day for > 4 weeks.

Steroid daily dose	Duration	Number of centres
= to or >5mg a day	3 months	2
8mg	6 months	1
20mg	6 months	1
0.5mg/kg	1 month	3
	2 months	1
	3 months	1
1mg/kg	at initiation	1
	> 1 month	3
	>2 months	1
	3 month	1
	6 month	1*
>1mg/kg	>1 month	2
	6months	1*
2mg/kg	> 1 month	1*

Table 1: GC dose and duration to trigger DXA scanning in context of HCT
* indicates paediatric centre

Management of reduced bone density

The most frequently cited management options for osteopenia were calcium/vitamin D (54/91 responding centres) and calcium/vitamin D together with bisphosphonates (24/91 including 3/11 responding paediatric centres). The most frequent treatment schedules for

osteoporosis were: bisphosphonates together with calcium/vitamin D (30/73 responding centres, including 4/9 responding paediatric centres), calcium/vitamin D alone (16/73, including 4/9 paediatric centres) and bisphosphonates alone (17/73, including 1/9 paediatric centres). Patients were more likely to be referred to other specialist teams for management input if they had osteoporosis (6/73 responding centres) compared to osteopenia (2/91 responding centres).

Use of bisphosphonates to maintain bone mineral density in absence of osteoporosis

Of 70 centres which responded, 41 indicated that they did not use bisphosphonates in the absence of osteoporosis. In two centres the reason given was that insurance companies would not cover its use in this setting. 27/29 centres which indicated that they do give bisphosphonates in the absence of osteoporosis also cited a reason for doing so with 4 centres giving two reasons. These were as follows: use of GC (n=13), patients with cGVHD receiving GC (n=4), GVHD alone (n=2), multiple myeloma (n=4), prior vertebral fracture (n=1), premature ovarian failure (n=1), recommendation by non-haematology specialists (n=4). Two paediatric centres indicated that they would consider pre-emptive bisphosphonates in a patient with osteonecrosis or high risk of avascular necrosis.

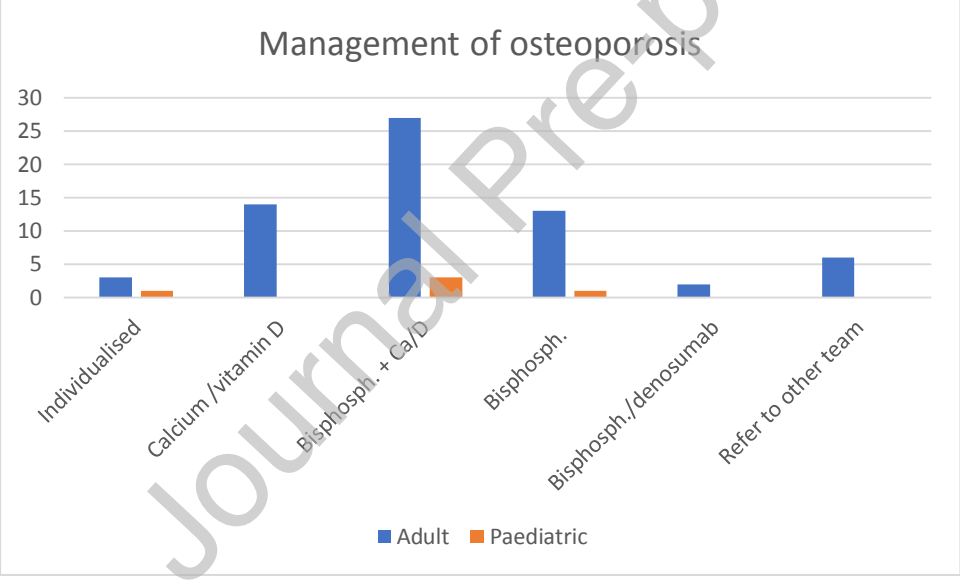

Figure 4: Treatment schedules for managing osteoporosis
Abbreviations: Bisphosph. = bisphosphonates; Ca = calcium; D = vitamin D

Use of guidelines

Respondents were asked specifically whether they had a local, national or international guideline to direct their practise and also whether there were any specific publications on which they based their practise.

Of the 79 centres that responded, the majority (51/79) had a local guideline relating to DXA scanning. Fewer than 20 centres used a specific publication (12/70 responders), national guideline (10/74 responders), or international guideline (15/72). The centres who conducted regular DXA scans were much more likely to use/have access to guidelines: of 52 centres who conducted regular DXA scans, 49/52 (94%) reported use of guideline compared to 18/47 (38%) centres who did not undertake regular DXA scans. Among the latter, local guidelines were used in the majority (16/18) with only two centres using publications to guide their practise.

Of 15 centres who used national/international guidelines or publications, 13 gave details.

Guidelines and publications used by responding EBMT centres	**N = (Ref)**
Recommended screening and preventive practice. Majhail *et al.* 2012	8 (25)
Consensus Statement of the German-Austrian-Swiss GVHD consortium. Hautmann *et al.* 2011	2 (26)
Recommended screening and preventative practice. EBMT/CIBMTR Rizzo *et al.* 2006	2 (27)
Osteoporosis Prevention, Diagnosis, and Therapy. NIH Consensus Development Panel 2001	2 (31)
Official positions from The International Society for Clinical Densitometry (ISCD)	2
Clinical report - Bone densitometry in children and adolescents - Bachrach *et al.* 2011	1 (32)
Pediatric Bone densitometry. Havrda. Radiologic Tecnology 2012*	1 (33)
EBMT handbook	1
ASH haematology education book 2010	1
NICE guidance on osteoporosis prevention (UK)	1
Coverage by insurance companies	1
Belgian bone club	1
Italian regional guideline	1

Table 2: Guidelines and/or publications used by EBMT centres participating in this survey

In some cases only partial details were given which did not enable identification of the publication in question. Nonetheless it was clear that in addition to HCT-related guidelines there were multiple non-haematological sources of guidance including endocrine, densitometry and osteoporosis societies and also guidance from insurance companies. The median number of different guidelines cited by each of 13 centres who gave details was 2 (range 1-3). The most frequent guideline referred to by 8/13 different centres was an international guideline on screening and preventive practices for long-term survivors after HCT published in 2012, representing a joint statement from multiple haematopoietic transplant organisations across the world (25). Of 8 centres which cited this paper as guiding their practise, triggers for DXA scanning were variable with two centres screening all patients, three centres screening all allografts, one screening female allograft patients over the age of 60 and a further two centres screening only patients with risk factors for low BMD.

The role of national policy/insurance companies in decision making

Data was available for 13/25 countries including 8/8 countries where there were several (5 or more) participating centres (figure1). The responses therefore applied to 82/99 (83%) participating centres in this study and for the majority of these there were no national policy or insurance restrictions to conducting DXA scans in patients at risk of low BMD in the context of HCT. Only one responding country (including 3 participating centres) indicated national policy restrictions for DXA scanning with an opportunity to conduct DXA scans restricted to once every 5 years. Three countries (including 17 centres) indicated that bisphosphonates were unlikely to be funded for the treatment of osteopenia by the majority of their insurance companies. Within each of the 8 countries with more than 5 centres, the approach to investigating and/or managing low BMD was inconsistent between participating centres irrespective of whether there were external policy restrictions to clinical decision making.

Discussion

The data presented in this study highlight considerable variation in the approach to investigating and maintaining bone health in both adult and paediatric centres after HCT. Attention to maintaining bone health through lifestyle advice was high in responding centres at approximately 80% for both adult and paediatric centres. Furthermore the majority of responding centres (65%) had local guidelines which included bone health. There was substantial variation, however, in the use of DXA scanning as a tool to guide management. Almost half the participating centres did not have routine triggers for DXA scanning. Amongst those that did the indications were variable with 11% responding centres scanning all transplant recipients, 20% scanning all allograft recipients and 28%

scanning patients who had received GC after transplant +/- before. Although receiving GC was the most frequent indication, the dose and duration triggers for prompting DXA evaluation were variable.

To some extent the variability seen amongst centres is reflective of some heterogeneity in existing transplant-follow up guidelines both in relation to who is screened and also when the screening should take place. In the most frequently cited guideline by participants in this study (25), DXA screening was recommended for all *allogeneic* transplant recipients (adult and paediatric), and in addition all female patients and those at high risk of bone loss. The latter were defined as those with the following: low BMI, physically inactive, hypogonadism, secondary hyperparathyroidism or who have received extended GC before or after transplant. A second guideline specifically tailored to bone health after HCT recommends screening *all* adult HCT recipients (allogeneic and autologous) after HCT with referral of paediatric HCT recipients to a paediatric endocrinologist (28). A previous consensus guideline from the CIBMTR, ASBMT and EBMT which was also cited by some participating centres in this study recommends DXA scans in adult women and those with prolonged glucocorticoids/calcineurin inhibitors (27). In relation to timing, the most frequently cited guidelines recommend DXA *at* one year post transplant (25,28,27) or else *within* one year (28) and recommend DXA are done 'sooner' in the presence of additional risk factors such as GC. Meanwhile, the Childrens Oncology Group long term follow up guidelines which include recommendations for children receiving HCT, recommend evaluation of BMD at entry into long term follow up which is typically two years after completion of cancer therapy (29).

Guidelines on bone health after transplant invariably highlight the significant negative effect of GC. In keeping with this, the largest single trigger for DXA scanning in this study was use of GC after (25% centres) and/or before HCT (total 28% centres). The dose of GC triggering concerns about bone health is quoted as greater than or equal to 5mg prednisolone for a duration > 3 months or 'long term' in the most frequently cited publications guiding our responders (25,26,28). In our study, however, 19 different GC treatment schedules were quoted as triggers for evaluation for BMD and a minority of centres (n= 2) indicated that they would arrange a DXA scan for a patient receiving 5mg (or more) a day of prednisolone for > 3months (Table 1). A systematic review investigating osteoporosis management among chronic GC users also described multiple duration and/or dose schedules used to define 'chronic GC use' (34). In our study some of the variation is likely to reflect the heterogeneity of dose schedules in the non-haematology literature particularly as non-haematological publications were regularly cited. Where GC are entered as a risk factor in the FRAX tool, the calculation is based on prednisolone doses in the range 2.5mg -7.5mg (17). An adjustment can be made for higher doses (> 7.5mg/day) but this may underestimate the risk of fracture associated with very high doses (35). Guidelines from the American College of Rheumatology have proposed different steroid dose cut-offs (5mg or 7.5mg of prednisolone) depending on whether a patient is at high or moderate risk for fracture and in addition draw attention to the risks of high cumulative doses of GC (36, 37). Data from population studies indicate that in adults greater than 40y of age total cumulative dose >1G are associated with an increased risk of fracture; a daily dose >30mg a day with a cumulative dose >5g confers a further increased risk (RR 14.4) (38, 39).

Multiple risk factors for low BMD have been described (25,40) and consistent with this in our data a number of different risk factors were considered as triggers for DXA scanning. However, almost half the centres responding to this survey did not consider any risk factors in their decision making and in 15 centres where risk factors alone were a trigger for DXA scanning, the median number of risk factors considered was low at three.

Guidelines indicate that management of established osteoporosis in adult survivors of HCT is similar to non-transplant populations and a combined approach with both bisphosphonates and calcium/vitamin D is recommended based on clinical trial data. Nonetheless this approach appeared under-utilised amongst participating adult centres in this study (41% responding centres). This may have reflected the ages of the patients undergoing transplant, because the use of bisphosphonates is controversial in children or females of child-bearing age. Denosumab was mentioned infrequently compared to bisphosphonates in this study which is in keeping with the fact that while there have been several randomised studies and a meta-analysis investigating the use of bisphosphonates in patients undergoing HCT (24) there is a lack of randomised data using denosumab in this patient group. Non-pharmacological measures are particularly important in these patients and include weight-bearing exercise, adequate dietary intake of calcium and vitamin D and assessment for and treatment of any underlying endocrinopathy/ hypogonadism.

Of 70 responding centres 31% indicated that they would consider using bisphosphonates pre-emptively in patients who did not yet have osteoporosis. The most frequent reasons given were use of GC and/or GVHD. This is in keeping with recommendations from the American College of Rheumatologists that bisphosphonates together with Ca/vitamin D can be used in patients commencing doses of steroids >5mg/day where the duration is likely to exceed three months (38). Furthermore it accords with the FRAX tool which recommends bone protection therapy in high risk patients (with the caveat of caution in women of childbearing age) even where DXA scan data is not available. In patients receiving HCT a meta-analysis of 12 studies (n=643 participants) concluded that bisphosphonates were promising in both preventing and treating bone loss following HCT (24). Despite these data, however, several participating centres were subject to insurance company restrictions that limited their prescription of bisphosphonates in the absence of a clear diagnosis of osteoporosis.

The majority of responding centres had local guidelines relating to bone health. Notably, centres which conducted regular scans were more likely to have a local guideline (94%) and also to use a national/international guidelines or a publication (25%, 13/52) to guide their practise than those that did not (38% and 4% respectively). Among centres which were aware of long term follow up guidelines, there was heterogeneity in the way that centres appeared to respond to them indicating poor engagement with their content. A lack of familiarity with long term follow up (LTFU) guidelines is not unique to transplant-physicians. In a mailed survey to paediatric oncologists in the United States of America only 33% respondents correctly answered three vignette based questions linked to LTFU guidelines (41). A disconnect between guidelines and management of bone health in patients receiving oral GC has been a feature of several published studies. A review of 29 such studies indicated that <40% patients receive appropriate BMD testing or pharmacological intervention (34).

We can only speculate as to the cause of the apparently poor engagement with low BMD as a complication of HCT. It may be that as early literature on this subject hinted at improvement in BMD without intervention (7) and evidence of fracture risk in small studies was low/inconsistent (43,44) the topic failed to attract attention. In the last 5 years, however, there have been several studies which have heightened concerns about bone health in the context of HCT. A large study including more than 7000 recipients of HCT, described fractures in approximately 8% patients (23). For survivors in the age range 45-64y the rate of fracture was approximately 8 times higher than the background population. An additional study in which 148 patients had prolonged follow up (median 12 years) has confirmed persistence of low BMD after HCT with a high prevalence of osteopenia (58%) and osteoporosis (18%) 3-5 years after HCT. A trend of improvement commenced only 10-15 years after transplant (45).

Recent guidelines/recommendations post-dating the time frame of this study have moved towards more aggressive monitoring of bone health. A multi-disciplinary working group on bone health and cancer concluded that patients undergoing allogeneic HCT should have a DXA at the hip and spine prior to HCT and radiological evidence of prior fracture sought (45). A recent paediatric guideline also recommends imaging prior to HCT (DXA at lumbar spine and total body) and regular screening for vertebral fracture (30).

It is possible that the complexities of investigating and managing a non-haematological condition early in the transplant process when the risks of mortality from the underlying haematology condition are a dominant consideration contributes to disengagement with this topic. The cost-effectiveness of early screening needs to be formally evaluated.

There are several limitations to this study. Firstly there was a low response rate of 22%. It seems probable that there was a response bias in favour of centres who were interested in bone health and this may have underpinned the relatively large number of participating centres that had local guidance about bone health and that gave lifestyle advice to promote bone health. If this was the case, it makes the apparent lack of awareness of risk factors for low BMD and lack of familiarity with current guidelines particularly striking.

A further limitation of this study is that we are unable to see the full extent to which national policy and insurance company restrictions may have played a part in decision making within all participating centres. Nonetheless, data representing 83% participating centres indicated that the majority had the freedom to follow existing guidelines Furthermore, It is clear from our data, that we cannot attribute the substantial heterogeneity of practise seen among EBMT centres to these potential restrictions because we did not see uniformity of practise within any of the 8 countries represented by multiple (5 or more) responding centres.

Conclusion

This study draws attention to the challenges of recognising and managing a non-haematological condition that has the potential to impact early in the post- transplant transplant clinical course. Robust cost-effectiveness data supporting pathways for identifying and managing low BMD in this group of patients may assist implementation of this aspect of care. While many centres registered with the EBMT are aware of bone health as an issue after transplant, there is inconsistency in practise in relation to screening for low BMD and also to managing low BMD. To some extent this reflects lack of familiarity with guidelines, but also it appears to be symptomatic of the myriad of guidelines that exist on this topic across a variety of disciplines. This highlights the need for development of a multidisciplinary guideline with input from all relevant stakeholders and education to improve familiarity.

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