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Glucocorticoid-Induced Osteoporosis Prevention in Polymyalgia Rheumatica Patients

T. Swami[1], C. Molloy[1,2]

1. University College Cork School of Medicine, Cork, Ireland
2. Department of Rheumatology, Cork University Hospital, Cork, Ireland

Abstract

Aim
Studies indicate that <50% of polymyalgia rheumatica (PMR) patients receive bone protective therapy (BPT) forglucocorticoid-induced osteoporosis (GIOP) prevention. We sought to determine if PMR patients are protected fromGIOP by examining bone densitometry (DXA) scan results, BPT use, and adherence to guidelines.

Methods
PMR patients treated with glucocorticoids who underwent a DXA scan at Cork University Hospital from 01/01/2016 to27/10/2017 were included. Patient data were obtained from chart review.

Results
Out of 153 patients, 73 (47.7%) were taking BPT and 42 (27.5%) were not. At the most recent DXA scan, 42 (27.5%) had normal BMD, 84 (54.9%) were osteopaenic, and 27 (17.6%) were osteoporotic. In 91 individuals who underwent≥2 DXA scans, patients not receiving bisphosphonates were more likely to have BMD loss over time (p=0.022).

Discussion
Despite recommendations, many patients are not prescribed BPT. The results suggest that PMR patients in Cork arenot optimally protected from GIOP.

Introduction

Polymyalgia Rheumatica (PMR) is the second most common rheumatic disease in adults primarily affecting females over 50 years old[1]. Its peak incidence in the United Kingdom is approximately 2.3 per 1,000 patient-years between the ages of 70 and 79[2]. Majority of PMR cases are managed in the primary care setting but the care of PMR patients varies widely[3].

Glucocorticoids (GCs) are the standard of care, which typically provide quick and effective improvement in symptoms. However, the relapsing and remitting nature of this illness, often requires GC treatment for ≥2 years[3]. PMR is one of the most common indications for long-term GC therapy (>3 months) in the community, accounting for 22% of GC prescriptions in the UK[4]. Most patients are started on a dose of 12.5-25 mg per day of prednisolone/prednisone-equivalent. If symptoms do not resolve in a few days, the dosage may be increased[3].

GC adverse effects are common in PMR, occurring in approximately 50% of patients, and present a further challenge to management[5,6]. Osteoporosis, with resultant fractures, is one of the most morbid of these complications, especially considering given PMR patients are typically post-menopausal women already vulnerable to BMD loss. Just 3 months of GC therapy has shown to cause rapid decline in BMD loss detectable by bone densitometry (dual-energy X-ray absorptiometry [DXA]) scan[7]. For this reason, the Irish Osteoporosis Society recommend that patients expecting to take at least 5 mg of prednisolone per day (or equivalent) for at least 3 months, should undergo a DXA scan at the initiation of treatment and every 2 years afterward to trend bone density measurements[8].

The American College of Rheumatology (ACR) have developed the guidelines and recommendations regarding preventative measures for GC-induced osteoporosis (GIOP)[8]. Calcium plus vitamin D supplementation is indicated for all patients beginning GC therapy but bisphosphonates are recommended for the vast majority of patients initiating long-term GCs, which have shown to maintain BMD[9,10]. These guidelines are adhered to inconsistently in the literature. One study reported less than 1/3 of patients received calcium and vitamin D supplementation[10]. Another study investigating prevention of GIOP in PMR patients specifically, reported that less than 30% of patients received bisphosphonates upon initiation of GC therapy. Analyzing individual patient cases revealed that 92% of patients should have received osteoporosis prophylaxis if the ACR guidelines were adhered to[11].

The evidence presented above indicates that PMR patients on long-term GCs may not be sufficiently protected from GIOP. It is uncertain whether PMR patients initiating GC therapy are receiving bone protective therapies (BPTs), such as calcium plus vitamin D, bisphosphonates, or teriparatide.

The objective of this study was to determine whether or not PMR patients are protected against GIOP. This was explored by determining the prevalence of osteoporosis and osteopaenia in this patient group, correlating T-scores of patients' DXA scans and use of BPTs, and estimated level of adherence to current ACR guidelines.

Methods

This study protocol was approved in December 2016 by the University College Cork Clinical Research Ethics Committee of Cork Teaching Hospitals.

Participants in this study were patients with a documented diagnosis of PMR and a history of chronic GC use. Patients were included in the analyses if they underwent a DXA scan over a 22-month time frame (01/01/2016 to 27/10/2017) at the Cork University Hospital (CUH) Bone Densitometry (DXA) Department. Patients who had no documented history of GC use were excluded from the study.

A separate subanalysis was conducted for patients who underwent ≥2 DXA scans by 27/10/2017. The difference between the last and first T-scores were calculated to determine whether or not BMD decreased, increased, or stayed the same.

Patient information was collected from the DXA Department patient database in CUH, including: age, gender, height, weight, smoking status, previous fractures, other medical conditions, and medications, including BPT such as calcium, vitamin D, bisphosphonates, denosumab, parathyroid hormone, and strontium. DXA reports within the database were also obtained to determine the T-scores at each scan.

Statistical Package for Social Sciences (SPSS) was used to analyse the data. Simple descriptive statistics were used to analyse baseline demographics of patients, in addition to BMD category (using T-scores patients were determined to be normal BMD, osteoporotic, or osteopaenic) and BPT use (none, calcium or vitamin D, or guideline-adherent). The Pearson's χ^2 test was used for the binomial categorical variables, whether or not the patient was taking BPT, presence of normal or low BMD (using most recent T-scores), and evidence of radiologic BMD loss over time (either decreased or not decreased). The associated p-values are reported. An independent t-test compared mean T-scores obtained from patients' most recent DXA scans to determine the correlation between decreased BMD and BPT use.

Results

Patient Demographics

Table 1 outlines the demographics of PMR patient identified for in this study. From 01/01/2016 to 27/10/2017, there were 182 PMR patients who underwent DXA scans, of whom 153 had a documented history of GC use at the time of their scan and were included in this analysis.

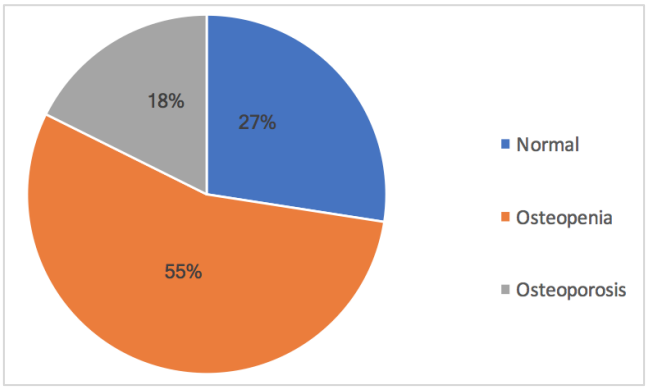
Table 1: Polymyalgia Rheumatica Patient Demographics

	N (%)
Total	153 (100)
Gender	
Female	105 (68.6)
Male	48 (31.4)
Age	
<50	1 (0.7)
51-60	16 (10.5)
61-70	45 (29.4)
71-80	68 (44.4)
>80	23 (15.0)
BMI	
Underweight (<19)	2 (1.3)
Normal (19-25)	36 (23.5)
Overweight (26-30)	68 (44.4)
Obese (>30)	47 (30.7)
Smoking Status	
Current/Previous Smoker	33 (21.6)
Non-Smoker	120 (78.4)
History of Adult Fracture	
Yes	55 (35.9)
No	98 (64.1)
Other Medical Condition*	
Yes	87 (56.9)
No	66 (43.1)

**Other medical conditions include: diabetes, chronic kidney disease, hypertension, heart failure, hyperlipidemia, coronary artery disease, hyper- or hypothyroid, history of cancer diagnosis, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, vasculitis, Crohn's disease, coeliac disease, asthma, COPD, epilepsy*

Figure 1 shows the prevalence of osteoporosis and osteopaenia within this group. On analyzing the most recent T-scores of individual patients, 42 (27.5%) had normal BMD (T-score > -1.0), 84 (54.9%) had osteopaenia (T score between -1.0 and -2.5), and 27 (17.6%) had osteoporosis (T-score ≤ -2.5).

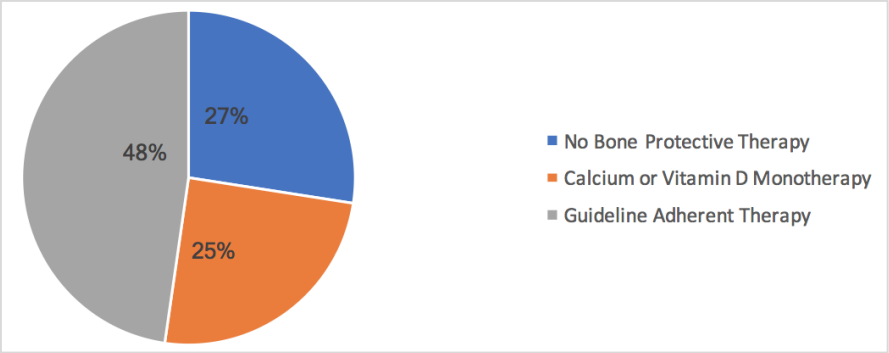
Figure 1: Prevalence of Osteopaenic and Osteoporotic Patients



Adherence to Guidelines

Out of 153 PMR patients, 111 (72.5%) were on some sort of bone protective therapy and of these, 38 were taking monotherapy calcium or vitamin D. Therefore, in total, 80 patients (52.3%) are not receiving guideline-adherent BPT and 73 (47.7%) are receiving BPT per current guidelines (Figure 2). Of these 73 patients, 44 (28.8%) patients were taking bisphosphonates, 8 (5.2%) patients were on denosumab, and 2 (1.3%) were taking Strontium.

Figure 2: Proportion of Patients on Guideline-Adherent Bone Protective Therapy



Correlations Between Bone Protective Therapies and Bone Mineral Density Loss

Of the 73 patients receiving BPT consistent with current guidelines, the mean T-score was -1.76 (SD=1.11). Of the 80 patients not receiving guideline-adherent BPT, the mean T-score was -1.41 (SD=0.97). There is a statistically significant difference between these (p=0.04, 95% CI -0.7 to -0.01) indicating that patients on BPT are significantly more likely to have a lower T-score. Of note, 15 (9.9%) patients had normal BMD and 58 (38.2%) were classified as osteopaenic or osteoporotic on their most recent DXA scan. Of the patients who were not receiving proper BPT, 27 (17.6%) were classified as having normal BMD, and 53 (34.6%) were classified as osteopaenic or osteoporotic. However, these findings were not significant (p=0.068).

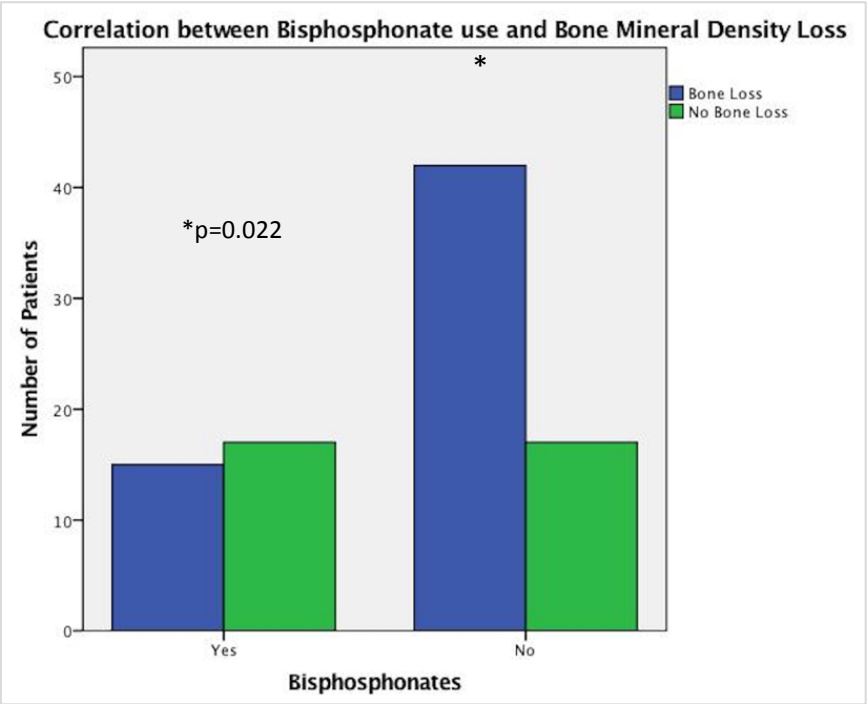
Subanalysis: Associations between Bone Protective Therapy Use and BMD loss over time in patients who underwent ≥2 DXA Scans

In total, 91 (59.5%) patients have undergone at least 2 DXA scans, of whom 57 (62.6%) experienced a decreased T-score from their first and last DXA scan representing a loss in BMD, while 34 (37.4%) did not show BMD loss.

Of the 91 patients who underwent serial DXA scans, 51 (56.0%) were taking BPT and 40 (44.0%) were not. On examining the patients taking BPT, 29 (31.9%) patients experienced bone loss over time and 22 (24.2%) did not. Of the patients who were not receiving BPT, 28 (30.8%) patients experienced bone loss over time and 12 (13.2%) patients did not. However, these differences are not significantly significant (p=0.199).

When looking specifically at bisphosphonate use and BMD loss over time, there was a statistically significant difference when looking at individuals who underwent ≥2 DXA scans (Figure 3). Of patients on bisphosphonates, 15 (16.5%) experienced BMD loss compared to 17 (18.7%) who did not. Of the patients not on bisphosphonates, 42 (46.2%) experienced BMD loss compared to 17 (18.7%) who did not (p=0.022). This indicates that patients not taking bisphosphonates were significantly more likely to experience BMD loss compared to patients who were taking bisphosphonates.

Figure 3: Correlation between Bisphosphonate use and Bone Mineral Density Loss over time.



Discussion

The prevention of GIOP with BPT is recommended for patients who are to receive ≥3 months of ≥7.5 mg of prednisolone or equivalent per day. BPTs that have shown effectiveness for this indication include calcium plus vitamin D, bisphosphonates, denosumab, and teriparatide[12]. Per current guidelines, approximately 92% of PMR patients should be put on GIOP prophylaxis[11].

In the literature, adherence to guidelines is varied. Two studies reported approximately 60% of PMR patients received osteoporosis prophylaxis[13,14], while another reported 48%[11]. One Japanese cross-sectional study noted that only 23% of physicians adhered to the Japanese GIOP prevention guidelines. However, this adherence increased to 57% if the GC dose exceeded 7.5 mg of prednisolone per day[15]. This is comparable to our study, revealing an adherence rate of 52%.

Interventions to encourage BPT prescription in patients taking long-term GCs have been attempted[16]. A Dutch randomized control trial investigated whether reminders from pharmacists to physicians prescribing GCs to also provide BPT would improve prescription of bisphosphonates. However, pharmacist contact did not significantly improve prescription of bisphosphonates after a 6-month follow-up period.

Additionally, it appears that patients who are prescribed BPT may not be receiving adequate protection. This is evidenced by the significantly lower T-score in patients who are taking BPT, in addition to 73% of patients having T-scores consistent with osteopaenia or osteoporosis. However, this observation is limited by the cross-sectional nature of this study, where the temporality between BMD loss and use of BPT cannot be concluded. As such, we cannot conclude if patients developed BMD loss prior to or after initiating BPT or glucocorticoid use.

The subgroup analysis examining patients who received ≥2 DXA scans show that majority of patients not taking bisphosphonates experienced BMD loss over time. A meta-analysis that investigated 9 randomized control trials reported that bisphosphonates increased BMD in the lumbar spine, total hip, and trochanter when given for prevention of GIOP[17].

A limitation in this study pertains to patient compliance. One cross-sectional study conducted in Denmark reported that compliance to BPT in PMR patients was 89%[18]. Unfortunately, BPT compliance could not be determined from our data and is a potential limitation in our study.

Several studies have examined the use of DXA scans in patients taking GCs to monitor for BMD loss. Consistently, it appears that, BMD monitoring through DXA scans, are not commonly performed[15,19,20]. Since our patient group only considers patients who underwent a DXA scan, it is possible that the PMR patients in our analysis were limited to individuals with ready access to CUH, which calls into question the generalizability of our results.

Additionally, there was no information in the database regarding glucocorticoid dosing or when the glucocorticoid was initiated. As such, we cannot determine whether these factors played a role in DXA scan results or correlated with BPT use and remains a confounding variable here.

To date, this is the only study that has examined the effectiveness of GC-induced osteoporosis GIOP prevention in PMR patients in Ireland. Here, we have demonstrated that there is a gap in the management of PMR patients, which exposes an opportunity for improvement in these patients. Future directions should be aimed at reaching out to the General Practitioners of individual patients to determine the dosing of GC and when it was initiated, in addition to confirming prescription of BPTs and identifying trends in medication compliance.

Declaration of Conflicts of Interest:
The authors declare that there is no conflict of interest.

Corresponding Author:
Tara Swami
University College Cork
Brookfield Health Sciences Complex, Rm 2.59
Brookfield, College Road
Cork, Ireland
T12 K8AF
Email: t.swami@umail.ucc.ie

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