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CLINICAL RESEARCH ARTICLE

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Fracture risk and impact in boys with Duchenne muscular dystrophy: A retrospective cohort study

Joshua Liaw MBBS Hons[1,2] | Natassja Billich PhD[3,4] | Kate Carroll PhD[1,3,5] | Justine Adams BPhysio[1] | Monique M. Ryan MMed, BS[1,3,4,6] | Eppie M. Yiu PhD[1,3,6] | Margaret Zacharin MBBS[1,6,7] | Peter Simm MBBS Hons[1,6,7] | Zoe E. Davidson PhD[1,3,4]

[1]Murdoch Children's Research Institute, Melbourne, Victoria, Australia

[2]James Cook University, College of Medicine, Townsville, Queensland, Australia

[3]Royal Children's Hospital, Neurology Department, Melbourne, Victoria, Australia

[4]Monash University, Department Nutrition, Dietetics and Food, Melbourne, Victoria, Australia

[5]Monash University, Department of Physiotherapy, Melbourne, Victoria, Australia

[6]University of Melbourne, Department of Paediatrics, Melbourne, Victoria, Australia

[7]Royal Children's Hospital, Endocrinology Department, Melbourne, Victoria, Australia

Correspondence
College of Medicine and Dentistry, James Cook University, Townsville QLD 4814, Australia.
Email: joshua.liaw@my.jcu.edu.au

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Abstract

Introduction/Aims: Boys with Duchenne muscular dystrophy (DMD) are at increased risk of fracture. This study investigated the incidence of fractures, factors contributing to risk of first fracture with emphasis on body mass index (BMI), and the impact of fractures on functional capacity in an Australian cohort of boys with DMD.

Methods: A retrospective cohort study included boys with DMD who attended a pediatric neuromuscular clinic from 2011 to 2018. Information regarding fractures, anthropometry measurements, body composition and functional assessment was collected. Factors associated with first fracture risk were analyzed with Cox-proportional hazards. Longitudinal analysis of function post-fracture was also conducted.

Results: This study included 155 boys with DMD. At least one fracture occurred in 71 (45%) boys; overall incidence of fractures was 399-per-10,000 persons-years. The first fracture was vertebral in 55%; 41% had non-vertebral fractures and 4% had both. Vertebral fractures occurred in significantly older (12.28 vs 9.28 y) boys with longer exposure to glucocorticoids (5.45 vs 2.50 y) compared to non-vertebral fractures. Boys with a history of fracture(s) had a steeper rate of functional decline (measured by Northstar Ambulatory Assessment score) than those with no recorded fractures.

Discussion: A high fracture burden was observed in a large Australian cohort of boys with DMD. Further investigation is required to understand preventative strategies and modifiable risk factors to reduce the incidence of fractures in DMD. The impact on fractures on ambulatory capacity should be closely monitored.

Abbreviations: BMD, bone mineral density; BMI, body mass index; DMD, Duchenne muscular dystrophy; DXA, dual energy absorptiometry; EK2, Egen Klassifikation 2; IQR, interquartile range; NSAA, Northstar Ambulatory Assessment; RCH, Royal Childrens Hospital, Melbourne; VF, vertebral fracture.

KEYWORDS
fractures, growth disorders, incidence, mobility, muscular dystrophy, osteoporosis, osteoporotic fractures, treatment outcome

1 | INTRODUCTION

Boys with Duchenne muscular dystrophy (DMD)experience increasing weakness and functional deterioration with age.[1] Fractures are reported to occur in 27–43% of boys with DMD, and can often have a detrimental impact on independent mobility and quality of life.[1–3] Major contributors to fractures in boys with DMD are falls due to weakness,[4] prolonged immobilization,[4] and glucocorticoid-induced osteoporosis, particularly in vertebral bone.[5]

As life-expectancy continues to improve for boys with DMD, fracture prevention and prolonging functional capacity in DMD are important considerations of care. There is increasing literature on interventions to reduce fracture risk, including glucocorticoid optimization[6,7] and bisphosphonate[8] administration during adolescence. Glucocorticoids are a mainstay disease-modifying treatment and are commenced when a child has noticeable slowing in motor gains, more frequent falls, or tires easily before substantial physical decline.[6] However, long-term, high dose glucocorticoid treatment causes linear growth failure, excessive weight gain and decreased bone density.[1,9] In Australia, prednisolone is the initial glucocorticoid therapy for boys with DMD, as deflazacort is not approved in Australia and only available to patients via a special access scheme. While early evidence was conflicting, more recent evidence suggests there is no significant difference in motor function outcomes or fracture rates between the two glucocorticoids.[7]

Recent studies on the use of prophylactic bisphosphonates have been optimistic.[8] The impact of nutrition and body weight optimisation, however, is much less studied and under-represented. Obesity increases fracture risk in all children,[10,11] but the effects of body mass index (BMI) on fracture risk in boys with DMD are less clear.[12] The increase in fat mass with age and inverse loss of lean mass is consistent with the progression of DMD.[13] Obesity in DMD can result from long exposure to glucocorticoids and reduced physical activity.[14] Mutations in the dystrophin gene also likely affect muscle metabolism directly.[13,14] The impact on fracture events on long-term ambulatory function is also poorly defined and identifying areas to prevent common mechanisms of repeat fracture events can also help guide clinical care.

This study aimed to determine the rate and characteristics of fractures in a cohort of Australian boys with DMD, identify factors contributing to risk of first fracture, and to assess the impact of fractures on functional capacity.

2 | METHODS

2.1 | Design and Setting

The Royal Children's Hospital (RCH), Melbourne provides the only pediatric multidisciplinary neuromuscular service in Victoria and is the largest single neuromuscular clinic in Australia. A retrospective review of boys with DMD managed at RCH was performed in 2018. Medical records were reviewed if the patient was seen in the clinic between January 2011 and July 2018.

2.2 | Participants

Patients were eligible if they had DMD and attended the neuromuscular clinic at RCH between January 2011 and July 2018. Cases were identified from clinic lists held by RCH. A diagnosis of DMD was confirmed by genetic testing and/or muscle biopsy in all cases. No age limit was set for participants, but the study only included data from a pediatric hospital. Those with insufficient medical records and clinical measures (i.e., attended only one clinic appointment) were excluded. Individuals with Becker muscular dystrophy were also excluded.

2.3 | Data Collection

Complete medical records of eligible patients were reviewed for data extraction. Data were collected via REDCap software (Vanderbilt University). REDCap forms were piloted among the research team to ensure reliability across researchers. Information on all cases including consultation notes, investigations results, scans, anthropometric data, and correspondence between clinicians were reviewed for relevant clinical outcomes. Follow-up was from the first visit at a neurologist appointment or date of diagnosis (whichever came first), until their last clinic visit or end of study period (July 2018). Reasons for discontinuation at the neuromuscular clinic included transfer to adult services, moved, lost to follow-up, attended an alternative clinic or died. Patients transition to adult services when they complete secondary schooling which is between the age of 18 and 20 y. Validation of data was performed by investigators in their respective fields of expertise; implausible or duplicate values were removed by consensus (N.B., J.A., K.C.).

Ethics approval was granted by the Royal Children's Hospital Research Governance Office (LNR/18/RCHM/233).

2.4 | Clinical Outcomes

Data on age at diagnosis, length of follow-up, glucocorticoid type (prednisolone, deflazacort) and regime (daily, intermittent), vitamin D supplements, and loss of ambulation were recorded. Fracture occurrence was confirmed by clinical documentation and/or radiological results reported in the medical record. Fracture type was stratified into vertebral (VF) or non-vertebral fractures (non-VF), lower limb

(femoral/hip, foot, ankle), upper limb (shoulder, humerus, wrist, fingers), or other/unspecified. When exact dates were not known for events, the first day of the documented month was recorded.

For each fracture, the presence of risk factors was assessed by collating clinical information up to 24 months prior to date of fracture. Suspected risk factors for fractures included age, BMI z-score, lumbar bone mineral density (BMD), body fat %, duration of glucocorticoid treatment, vitamin D deficiency and ambulatory status. The maximal BMI z-score documented for each boy with DMD between age 6 and 9 y was also recorded. An increased rate of weight gain can occur in boys with DMD from approximately age 7 y.[19] A small group of boys (n = 17) in this cohort was part of a randomized-control trial that assessed prophylactic bisphosphonates on bone health. Currently, prophylactic bisphosphonate use in boys with DMD is not standard care in Australia and is not funded by the national Pharmaceutical Benefits Scheme.

All boys commencing glucocorticoid treatment for DMD were initially prescribed prednisolone (initial dose ~0.75 mg/kg/d). Some subsequently switched to deflazacort (0.9 mg /kg/d) due to poor efficacy or unfavorable side effects (usually behavioral or weight-related). Boys received only one type of glucocorticoid at any time and both daily and intermittent dosing regimens were used. Anthropometric data (height and weight) were used to calculate BMI (weight kg/height m^2), which was then converted to BMI z-scores by Cole's LMS method using Centers for Disease Control and Prevention reference data.[15] Vitamin D deficiency was defined as a serum 25(OH)-D level < 50 nmol/L (<20 ng/mL). Body composition measures (lumbar BMD z-score, and body fat mass percentage) were collected by dual-energy X-ray absorptiometry (DXA) scanning.

Functional assessments were analyzed over time for boys above 7 y, as consistent decline in motor performance is observed after this age.[17,21] These assessments included timed function tests (10 m walk/run, supine-to-stand and four stairs ascend) and Northstar Ambulatory Assessment (NSAA) scores for ambulatory boys, and EK2 scores for non-ambulatory boys.

2.5 | Statistical Analysis

Data analysis was performed using SPSS, version 27.0 (IBM). Normality of data was determined by Shapiro–Wilk tests. Patient characteristics were described as median and interquartile range (IQR) of 25–75% or mean and standard deviation (SD) depending on normality, and frequency and percentage for categorical data. Fracture incidence rates were calculated per 10,000 person-years. Quantile regression with 95% confidence interval (CI) estimated the difference in medians for non-equally distributed independent samples. Kaplan–Meier graphs were used to evaluate the potential relationship between body-mass-index and first fracture probability according to age (years).

Log-ratios were used to compare the effects between subgroups; a *p*-value of <0.05 was considered statistically significant.

TABLE 1 Characteristics of all patients during this study (n = 155)

Category	All
Age at diagnosis in years	
Mean (SD)	4.18 (2.08)
Length of follow up in years	
Total sum of patient-years	1356 years
Mean (SD)	8.75 (4.7)
Glucocorticoid regimen	
None	16 (10%)
Prednisolone only	81 (52%)
Prednisolone then deflazacort	58 (38%)
Vitamin D	
Ever deficient in vitamin D (25(OH)-D < 50 nmol/L)	
No	27 (17%)
Yes	95 (62%)
Unknown	33 (21%)
Vitamin D supplementation	
No	50 (32%)
Yes	105 (68%)
Calcium supplementation	
No	81 (52%)
Yes	74 (48%)
Loss of ambulation	
Ambulatory status at end of follow up	
Non-ambulant	82 (53)
Ambulant	73 (47)
Age of loss of ambulation (years) n = 77	
Mean (SD)	11.1 (2.6)

Abbreviation: BMD, bone mineral density; BMI, body mass index; IQR, interquartile range (25%–75%).

Univariate and multivariate cox proportional hazards models with time-dependent covariates were used to investigate risk factors on time (age) to first fracture. The primary factors of interest were BMI during the age epoch 6–9 y, vitamin D deficiency, duration of glucocorticoid use, ambulatory status, and use of bisphosphonates prior to fracture. Univariant analysis was conducted, with factors of $p < 0.3$ included in multivariate analysis. Time-dependant covariates (duration of glucocorticoid use and bisphosphonate use were calculated in 0.25-y intervals and loss of ambulation status was time-adjusted for the age of first recorded loss of ambulation. Model goodness of fit was assessed with the −2- log-likelihood ratio test, with hazard ratios of 95% CI presented in the table.

Change in functional assessment pre- and post- first fracture were analyzed with Wilcoxon rank-sum test if adequate sample size was reached. Repeated NSAA scores of patients were compared between boys with a fracture and those without a fracture across age groups. A best fit line was determined by testing both linear and fractional polynomials. Pairwise deletion for cases with missing data was

TABLE 2 Characteristics of boys at the time of their first fracture

Characteristics of boys at the time of first fracture (n = 71 patients)	
Category	**Median (IQR)**
Age of first fracture	11.41 (5.3)
Duration of glucocorticoid use (years) at fracture	4.00 (4.8)
BMI (z-score)[a]	1.57 (1.5)
Body fat (%)[b]	39.3% (15.7)
Lumbar BMD (z-score)[c]	−2.4 (1.6)
Height adjusted lumbar BMD (z-score)[d]	−0.7 (1.4)

Abbreviation: BMD, bone mineral density; BMI, body mass index; IQR, interquartile range (25%–75%).
[a]Data missing in four patients.
[b]Data missing in 39 patients.
[c]Data missing in 39 patients.
[d]Data missing in 44 patients.

carried out for descriptive statistics, and list-wise deletion for the cox-proportional hazards model.

3 | RESULTS

A total of 155 patients were identified. Characteristics of this cohort are summarized in Table 1. Most subjects were glucocorticoid treated, with an average age of first dose at 6.6 (2.3) years. Seventeen (11%) boys were prescribed intermittent glucocorticoid dosing at some point. Ten boys (7%) died during the follow-up period; there was one death that resulted from fat embolus complications following a femoral fracture sustained in a fall from a wheelchair.

Of the 81 boys that received prednisolone only during the study, 12 received a period of intermittent prednisolone dosing. For boys that were initially taking prednisolone but changed to a deflazacort-only regimen, this change occurred at an average age of 8.60 y, with an average duration of prednisolone before the change of 2.68 y.

3.1 | First Fracture Occurrence

Of the 155 patients, 71 subjects (46%) had at least one fracture event. The incidence rate of fracture in this cohort of DMD was 399 per 10,000 person years. Baseline characteristics at the time of first fracture event are displayed in Table 2; a total of 80 fractures were recorded. (Figure 1). The overall probability of first fracture (non-VF and/or VF) was 19% by age 10, and 64% by age 20.

In terms of steroid regimen at the time of fracture, 48 boys (67%) had received prednisolone only regimens, and 20 boys (28%) received at least 3-mo of deflazacort prior to fracture (after their switch from prednisolone). Three boys (5%) had fracture events and never received steroids.

Testosterone supplementation was used in 28 boys after the age of 14; however, only four received dosing prior to fracture event (for an average 0.90 y); of the 24 boys remaining, 22 went on to have fractures and 2 boys never had a fracture event.

Bisphosphonate use was recorded in 53 boys, with an average age of first dose at 12 y. Eight boys received it prophylactically prior to fracture event, and nine boys that received bisphosphonates prophylactically never had a fracture event.

Of the boys that had more than one fracture site reported at their first event (n = 8), four had multiple non-VF, three had both VF and non-VF, and one boy sustained bilateral femoral fractures and a lumbar vertebral fracture in a fall from a wheelchair (aged 14 y).

Documentation about mechanism of injury was only available for 19 fractures; 8 were due to wheelchair-related falls, 7 from low impact falls from standing height, and 4 from other mechanical falls where exact mechanism was unclear (non-specific). Two boys reported a permanent loss of independent ambulation immediately after their first fracture event; both of which were lower limb non-VF.

Comparison of patient characteristics at time of first fracture between boys with a VF and non-VF (Table 3) showed those who sustained a VF were older and had a longer duration of glucocorticoid treatment by approximately 3 y. Lumbar BMD z-score was lower in boys with VF, but no difference was observed after adjustment for height. There was no statistically significant difference in BMI and body fat % between patients with VF vs non-VF; however, the median BMI was within the overweight weight range in the VF group and the obese range in the non-VF group.

No vertebral fractures were reported in the patients that never received glucocorticoids.

3.2 | Risk of First Fracture: Cox-Proportional Analysis

Following this, we further performed comparisons of first fracture risk with regards to the various prognostic factors as shown in Table 4. Only boys that received glucocorticoids were included in this analysis. Furthermore, glucocorticoid regimen was not analyzed due to inability to separate relative effects of prednisolone or deflazacort in boys that received both during the observation period.

Cox regression with time-dependant univariate analysis showed correlation between higher body-mass-index at age 6–9 and fracture risk. The length of time a patient received steroids was not significantly associated with fracture risk. No variables reached included in the multivariate analysis reached statistical significance.

3.3 | Boys with Multiple Fractures

Twenty boys with DMD had a total of 31 subsequent fracture events: second fracture (n = 20), third fracture (n = 6), fourth fracture (n = 4), and fifth fracture (n = 1). Second fractures occurred a median (IQR) of 2.68 (3.12) years after the first fracture. Vertebral fractures occurred in 48% (n = 15), femoral fractures in 23% (n = 7), and 29% (n = 9) were other non-vertebral fractures. No significant difference in

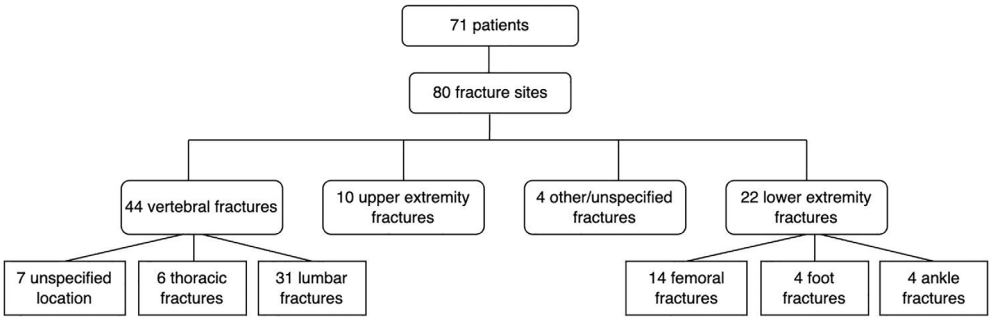

FIGURE 1 Composition of types of fractures. Four "Other/unspecified" fractures included one skull fracture from a fall out of wheelchair, and three unspecified fracture sites.

TABLE 3 Comparison of baselines between vertebral fractures and non-vertebral fractures[a]

	VF		non-VF (ref)		
Category	**n**	**Median (IQR)**	**n**	**Median (IQR)**	**Difference in medians (95%CI)[+]**
Age in years	39	12.28 (5.54)	29	9.28 (3.13)	3.00 (0.97, 5.03)
Duration of glucocorticoid use (in years)	39	5.45 (3.36)	29	2.5 (3.52)	2.95 (1.09, 4.81)
BMI z-score at time of fracture	38	1.40 (1.54)	26	1.86 (1.52)	−0.68 (−1.53, 0.17)
Body fat %	25	38.6 (15.7)	6	42.3 (13)	−4.00 (−20.83, 12.83)
Lumbar BMD z-score	29	−2.7 (1.3)	10	−1.7 (2.3)	−0.800 (−1.93, 0.32)
Height adjusted BMD score	21	−0.7 (1.2)	6	−0.7 (1.8)	−0.35 (−1.92. 1.21)

Abbreviation: BMD, bone mineral density; BMI, body mass index; CI, confidence interval; non-VF, non-vertebral fracture; VF; vertebral fracture, .
[a]Four patients had both VF and non-VF at time of first fracture and were excluded from analysis.
[+]Difference in medians with 95% CI calculated with quantile regression.

TABLE 4 Time-dependant cox-proportional model of time to first fracture event

		Univariate analysis				Multivariate analysis N = 113, event = 57		
Variable	**Event**	**n**	**HR**	**95% CI**	**p value**	**HR**	**95% CI**	**p value**
BMI age 6–9 continuous	58	114	1.24	1.00–1.56	0.05	1.23	0.98–1.54	0.07
Duration of steroid	61	124	1.00	0.99–1.00	0.76	NA		
Loss of ambulation	60	122	0.64	0.32–1.28	0.21	0.74	0.36–1.52	0.41
Vitamin D deficiency	53	103	1.30	0.73–2.32	0.38	NA		
Prophylactic bisphosphonate	61	124	1.21	0.89–1.65	0.22	1.10	0.78–1.55	0.60

Abbreviation: BMI, body mass index; Event, number of fracture events in that specific group (n); n, number of patients included in the analysis excluding boys with missing data (pair-wise); HR, hazard ratio; NA, not considered in the multivariable model; ref, reference.

ambulatory status, duration of glucocorticoid, BMD z-score, body fat % or BMI were identified between boys that had multiple incidences of fractures, compared to boys with only one incidence of fracture (Table S1).

3.4 | Functional Outcomes Pre- and Post- Fracture

There were limited matched data available on functional outcomes pre and post fracture. Data is reported descriptively due to the low numbers (Table S2). Boys who were non-ambulant (n = 6) had a higher median EK2 score (indicating decreased function) after first fracture event; from 7 pre-fracture to 12 by 2 y post-fracture. Two boys reported a permanent loss of independent ambulation immediately after their first fracture event; both were lower-limb non-VF. Boys who were ambulant (n = 15) also had a decline in NSAA score post-fracture; from 24 pre-fracture to 21 by 2 y post-fracture. There was no change in average timed function tests (10 m walk/run, supine-to-stand, and stair ascending time) in those with available data.

3.5 | Sub-analyses of Functional Decline in Ambulant Boys with NSAA Scores

Boys with DMD were separated into two groups: those who sustained a fracture and those who did not (Figure 2). Individual NSAA trajectories as well as the average NSAA slope of decline over time were described for both groups. Visual comparison of these graphs

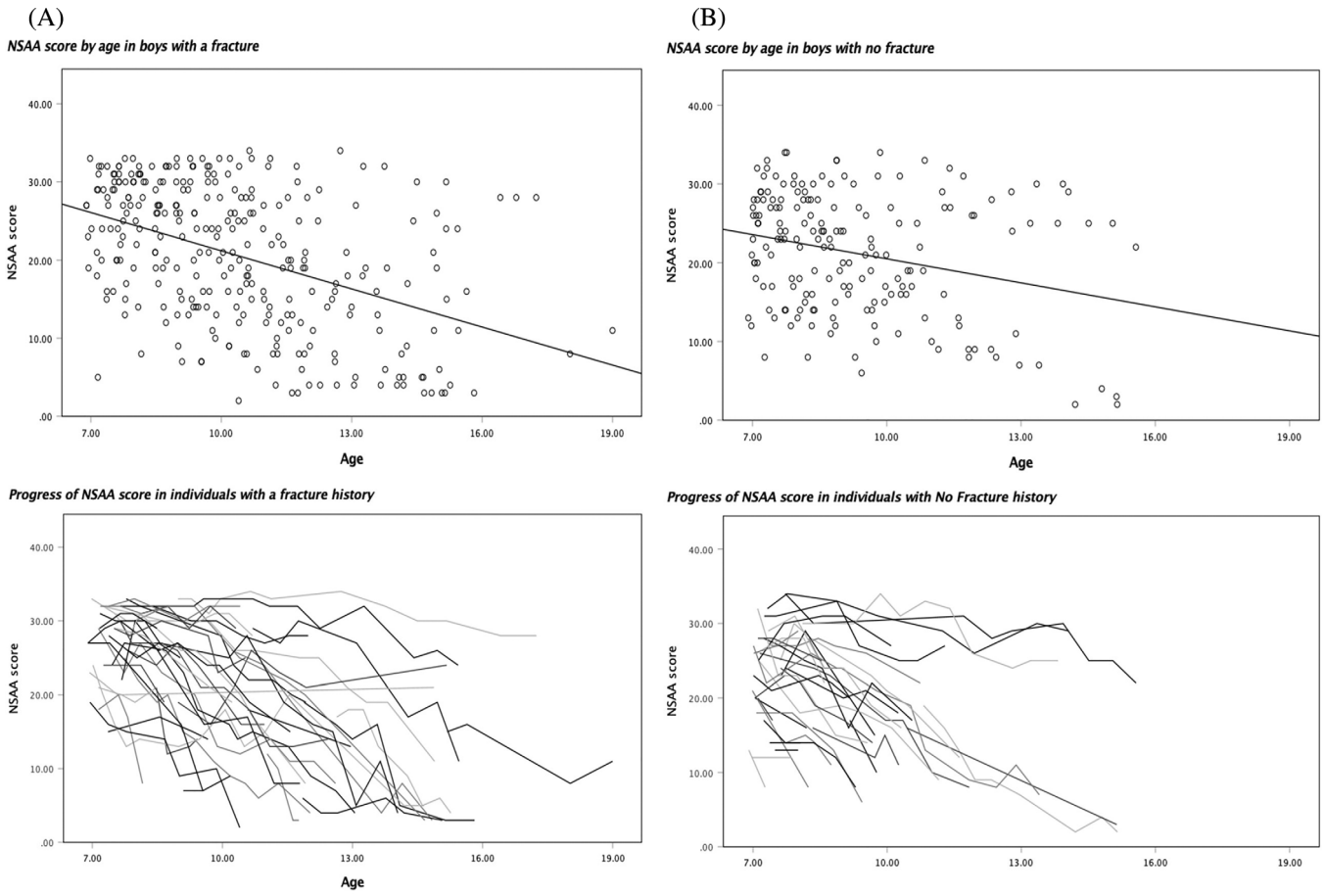

FIGURE 2 NorthStar Ambulatory Assessment Score by age in boys with Duchenne muscular dystrophy after 7 y of age for (A) patients that sustain a fracture, (B) patients with no fractures. NorthStar Ambulatory Assessment Score only included from age 7 y and above to minimize the impact of developmental gains that may occur prior to this age.[32]

suggests a general trend towards more rapid decline in boys with fractures, although this was a modest difference. In boys with a history of fracture event(s) (n = 366 assessments, 48 patients), NSAA scores declined on average by 0.44 points (95% CI: −1.55, −0.49) per year. In contrast, those with no fractures (n = 337, 53 patients), declined on average by 0.27 points (95% CI -1.55, −0.49) units per year.

4 | DISCUSSION

The fracture incidence in this study of 399 per 10,000 person years is almost 4.5 times higher than typically developing children in Australia (85 per 10,000 person years).[16] Overall fracture frequency was 44.9% in this cohort of boys with DMD, which is similar to other reports of DMD in Australia (43%)[2] and Europe (21%–48%).[1,3,17,18]

This study showed that, while longer duration of glucocorticoids was significantly associated with vertebral fractures as expected,[5,19] this was not the case for overall fractures events (combined non-VF and VF).

The only association that reached univariant significance was body-mass index; however, this was not independently significant in multivariant analysis. The nutritional issues associated with DMD are complex, poorly understood, and likely affected by multiple influences such as inherent disease progression, glucocorticoid dosage, and reduced mobility. Boys with DMD are at high risk for developing obesity.[20] In Australia, the prevalence of obesity reaches 50% of boys with DMD by age 10 y.[20,21] Similar trends are seen globally: studies report that by 13 y, weight > 90 percentile ranges from 44% to 73% in boys with DMD.[22]

While high BMI showed univariant relation to fracture risk, this needs to be interpreted with caution. This study does not infer an independent association of obesity with fracture risk as it did not adjust for the effect of individual steroid dosage or steroid regimen. Rather, we suggest that weight control should have greater focus, particularly its modifiable aspects, for optimizing bone health and other DMD-related outcomes.[21]

Mechanisms of how higher BMI can correlate with fracture rates, particularly lower limb fractures may include inappropriate adaptation of the axial skeleton with body size and impaired balance.[11,23] Unique to dystrophin deficiency, boys with DMD also exhibit progressive replacement of lean muscle mass with intramuscular adipose tissue; both reducing energy expenditure, increasing body fat mass, and impacting the structural integrity of the axial skeleton.

The importance of preventable interventions on weight management such as dietary optimization should not be underestimated. Previous studies have observed mismatches in caloric intake being excessive in pre-school and school-age groups.[14,23] Greater emphasis on weight-related strategies and regular nutrition counseling early in the disease course should be at the forefront of bone health in boys with DMD.[6,23] Further studies investigating the association of obesity on lower-limb fracture risk are needed, with emphasis on adjusting for the effects of steroid use (dosage, regimen, etc.). Furthermore, interventions to optimize caloric intake in boys with DMD would be beneficial.

Evidence for benefits of prophylactic bisphosphonates (i.e. zoledronic acid) for boys with glucocorticoid-dependent DMD is increasing.[8] Early treatment with bisphosphonates has shown to improve bone density after 24 mo[8]; however, evidence for benefit for new fracture incidence remains limited. Improved BMD may reduce vertebral fractures incidence[8]; however, further studies are required.

While this study cannot accurately compare the effects of glucocorticoid regimen choice on bone health and fractures, this outcome has been reported previously. A recent large multi-center randomized controlled trial found no significant difference in motor function, fracture rates, or weight gain between daily prednisolone and daily deflazacort; however, daily prednisolone did have a significantly greater increase in body mass index over time.[7] Boys on intermittent prednisolone have evidence of worse motor function outcomes, shorter time to loss-of-ambulation, but steadier BMI compared to daily regimens.[24] With only a small cohort on intermittent dosing (11%) in this study, we were unable to investigate this outcome.

This study also attempted to observe how fracture events affect long-term mobility outcomes. An increased rate of decline in NSAA scores in boys with a history of fracture compared to those with no fracture was seen. This supports evidence of significant function and ambulation loss after particularly lower limb fractures in boys with DMD,[24,25] While there are likely patient inherent factors that affect fracture recovery,[24] fracture management should aim to minimize prolonged immobilization and promote early rehabilitation. Regular post-fracture assessments may also help monitor clinical progression and allow for future studies of maintaining independent mobility for longer after major fractures.

No clinical indicator for predicting repeat fracture events was found in this study, mainly due to limited sample size. However, minimal trauma or low-impact injury (falls from wheelchair with no seatbelt) were commonly cited as mechanisms of fractures in this study. Proactive care strategies and education to carers and families on common high-risk environments or activities may help prevent fracture events.[26]

There were several other limitations with this study. Data collected retrospectively may lead to under ascertainment, especially if fractures were managed outside of the tertiary care setting. We were unable to adjust for all potential confounders in cox-proportional hazard analysis such as glucocorticoid regimen, cumulative glucocorticoid dosages, BMD z-scores, DMD phenotypes, and co-morbidities. Association of BMI and fracture risk in DMD should therefore be interpreted with caution, until further studies adjust for these factors, particularly glucocorticoids. Missing data restricted paired sample analysis of functional outcomes. Future observation at pre-defined intervals, or prospective study designs would be useful for longitudinal assessment of fracture rehabilitation. NSAA assessments were conducted over varied time intervals according to clinic attendance, and the unbalanced data limited comparative analysis. Missing data from detection bias may be present i.e. boys with a fracture event may be more frequently assessed, compared to ambulatory boys with no fracture events that have the same rate of NSAA decline.

5 | CONCLUSIONS

Boys with DMD have high rates of fractures compared to healthy controls, which may have lasting impact on function and quality of life. Early use of prophylactic bisphosphonates has been shown to improve BMD however the effect on fracture incidence should be further investigated. Similarly, further investigation on the effect of obesity on fracture incidence is needed. The impact of fracture events on the rate of functional decline in boys also requires further definition with functional assessment post-fractures. As life-expectancy continues to improve for boys with DMD, prolonging functional capacity and preventing fracture events is increasingly important.

AUTHOR CONTRIBUTIONS

Joshua Liaw: Formal analysis; investigation; methodology; visualization; writing – original draft; writing – review and editing. **Natassja Billich:** Conceptualization; data curation; resources; supervision; validation. **Kate Carroll:** Investigation; project administration; resources; supervision; validation; writing – review and editing. **Monique M Ryan:** Conceptualization; investigation; project administration; resources; supervision; writing – review and editing. **Justine Adams:** Investigation; resources; validation; visualization; writing – review and editing. **Eppie M Yiu:** Investigation; supervision; writing – review and editing. **Margaret Zacharin:** Investigation; supervision; validation; writing – review and editing. **Peter Simm:** Investigation; supervision; visualization; writing – review and editing. **Zoe E. Davidson:** Conceptualization; data curation; funding acquisition; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ORCID

Joshua Liaw https://orcid.org/0000-0002-7900-3938
Kate Carroll https://orcid.org/0000-0002-2519-3289

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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