PERSPECTIVE

Preliminary training volume and progression algorithm to tackle fragility fracture risk during exoskeleton-assisted overground walking in individuals with a chronic spinal cord injury

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CONTEXT

In individuals with chronic complete spinal cord injury, reduced lower-limb weight-bearing due to long-term manual wheelchair use, as well as neurological and vascular dysfunctions below the level of injury, contribute to the loss of bone mineral density [1]. Unfortunately, low bone mineral density is associated to reduced bone strength and increased risk of lower-limb fragility fracture in this population [1]. Wearable robotic exoskeletons are an emerging and rapidly progressing technology that has, among other things, the potential to significantly increase lower-limb weight-bearing (i.e., mechanical loading) in this population. Mechanical loading is an important factor influencing bone strength through the "*mechanostat*" principal [1]. Briefly, the forces exerted on bone tissue during mechanical loading trigger an anabolic state during which the osteocyte-lead bone formation surpasses the osteoclast-lead bone resorption—thus, strengthening bone [1]. Hence, research in overground exoskeleton-assisted walking programs has increased substantially recently as such interventions could potentially increase bone strength and, theoretically, reduce the risk of fragility fractures (and associated complications). However, reported cases of lower-limb fragility fracture during exoskeleton-assisted walking raise safety concerns for both rehabilitation clinicians and researchers [2–4].

To ensure that research on this novel technology can be conducted ethically and safely, there is a need to strike an optimal balance so that the potential benefits of exoskeleton-assisted walking programs outweigh their potential risks. To our knowledge, aside from a recent history of lower-limb fragility fracture and a demonstrated capability to tolerate static standing posture, there are currently no universally accepted criteria or manufacturer recommendations on how to safely engage individuals with low bone mineral density in exoskeleton-assisted walking programs [5]. Hence, rehabilitation researchers must rely on a trial-error process supported by their competencies, experience, and intuition to establish and progress walking program parameters, especially in terms of total walking time, number of steps, or distance traveled. Yet, very few studies involving exoskeleton-assisted walking have used cut-off values for bone mineral density threshold (i.e., hip or spine T-score < -2.0; total hip or femoral neck T-score < -3.5) to mitigate fragility fracture risk [6, 7]. Thus, this *Perspective* introduces a recently developed algorithm, based on bone mineral density, targeting the mitigation of fragility fracture risk in individuals with chronic spinal cord injury engaging in an overground exoskeleton-assisted walking program [8]. Ultimately, this paper aims to open a discussion and engage the clinical and scientific communities into the co-creation of a decisional algorithm, based on a consensus-building process, to assure patient safety as this novel technology continues to be studied and implemented.

DEVELOPMENT OF AN EARLY-STAGE ALGORITHM

The development of this early-stage algorithm was first informed by an overview of the literature conducted by AB and DHG [8]. This overview focused on lower-limb fracture risk in individuals with a spinal cord injury, as well as aerobic exercise recommendations, particularly walking, among individuals with neuromusculoskeletal impairments and functional disabilities. Thereafter, following the consultation of a preliminary version developed by AB and DHG, recommendations were formulated by experts in internal and physical medicine (SNM), rehabilitation (AB, DHG, MV, and ME), and adapted physical activity (MAL).

This early-stage algorithm aligns with the World Health Organization's bone mineral density criteria for osteoporosis and is summarized in Fig. 1 [9]. Total hip bone mineral density, measured by dual-energy X-ray absorptiometry, is used to classify individuals in one of three profiles: osteoporotic profile (T-score ≤ -2.5), osteopenic profile ($-2.5 <$ T-score < -1.0), or preserved bone mineral density profile (T-score ≥ -1.0). To mitigate lower-limb fragility fracture risk and other secondary walking-related musculoskeletal impairments: individuals classified in the osteoporotic profile are assigned to a slow-progression exoskeleton-assisted walking program that begins with a session maximum of 300 steps during the first week and increases by up to 10% weekly

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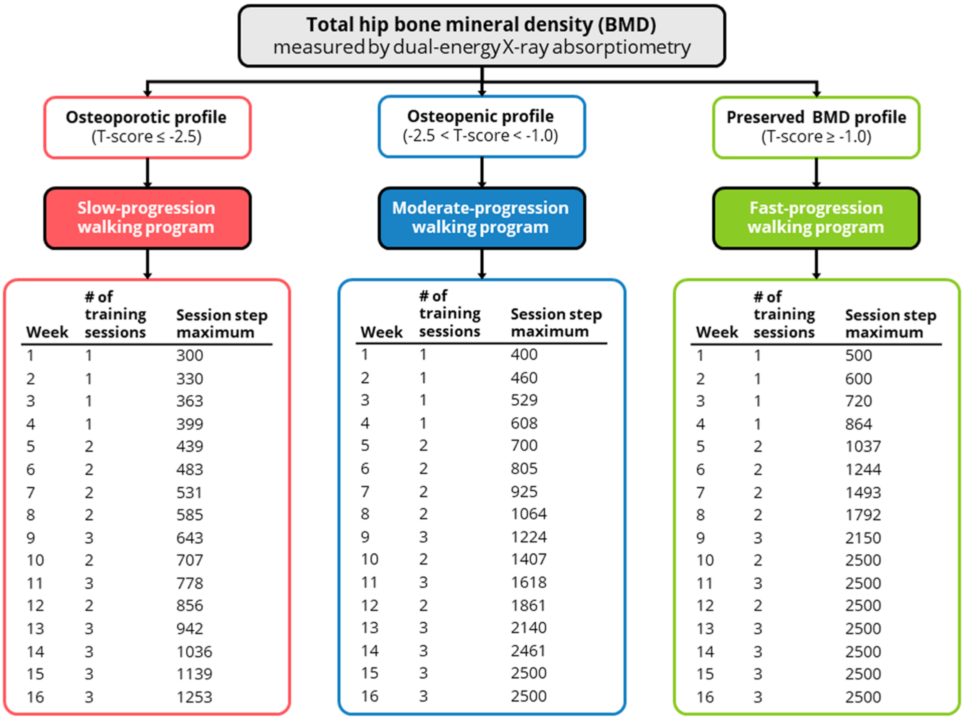


Slow-progression walking program

Week	# of training sessions	Session step maximum
1	1	300
2	1	330
3	1	363
4	1	399
5	2	439
6	2	483
7	2	531
8	2	585
9	3	643
10	2	707
11	3	778
12	2	856
13	3	942
14	3	1036
15	3	1139
16	3	1253

Moderate-progression walking program

Week	# of training sessions	Session step maximum
1	1	400
2	1	460
3	1	529
4	1	608
5	2	700
6	2	805
7	2	925
8	2	1064
9	3	1224
10	2	1407
11	3	1618
12	2	1861
13	3	2140
14	3	2461
15	3	2500
16	3	2500

Fast-progression walking program

Week	# of training sessions	Session step maximum
1	1	500
2	1	600
3	1	720
4	1	864
5	2	1037
6	2	1244
7	2	1493
8	2	1792
9	3	2150
10	2	2500
11	3	2500
12	2	2500
13	3	2500
14	3	2500
15	3	2500
16	3	2500

Fig. 1 Early-stage exoskeleton-assisted walking program clinical support algorithm. Early-stage algorithm aligned with the World Health Organization's bone mineral density criteria for osteoporosis. Total hip bone mineral density is used to classify individuals in one of three profiles: osteoporotic profile (T-score ≤ −2.5), osteopenic profile (−2.5 < T-score < −1.0), or preserved bone mineral density profile (T-score ≥ −1.0). Individuals classified in the osteoporotic profile are assigned to a slow-progression exoskeleton-assisted walking program that begins with a session maximum of 300 steps during the first week and increases by up to 10% weekly thereafter. Individuals classified in the osteopenic profile are assigned to a moderate-progression program that begins with a session maximum of 400 steps during the first week and increases by up to 15% weekly thereafter. Individuals classified in the preserved bone mineral density profile are assigned to a fast-progression program that begins with a session maximum of 500 steps during the first. The number of training sessions per week also increases during the 16-week period included in the algorithm.

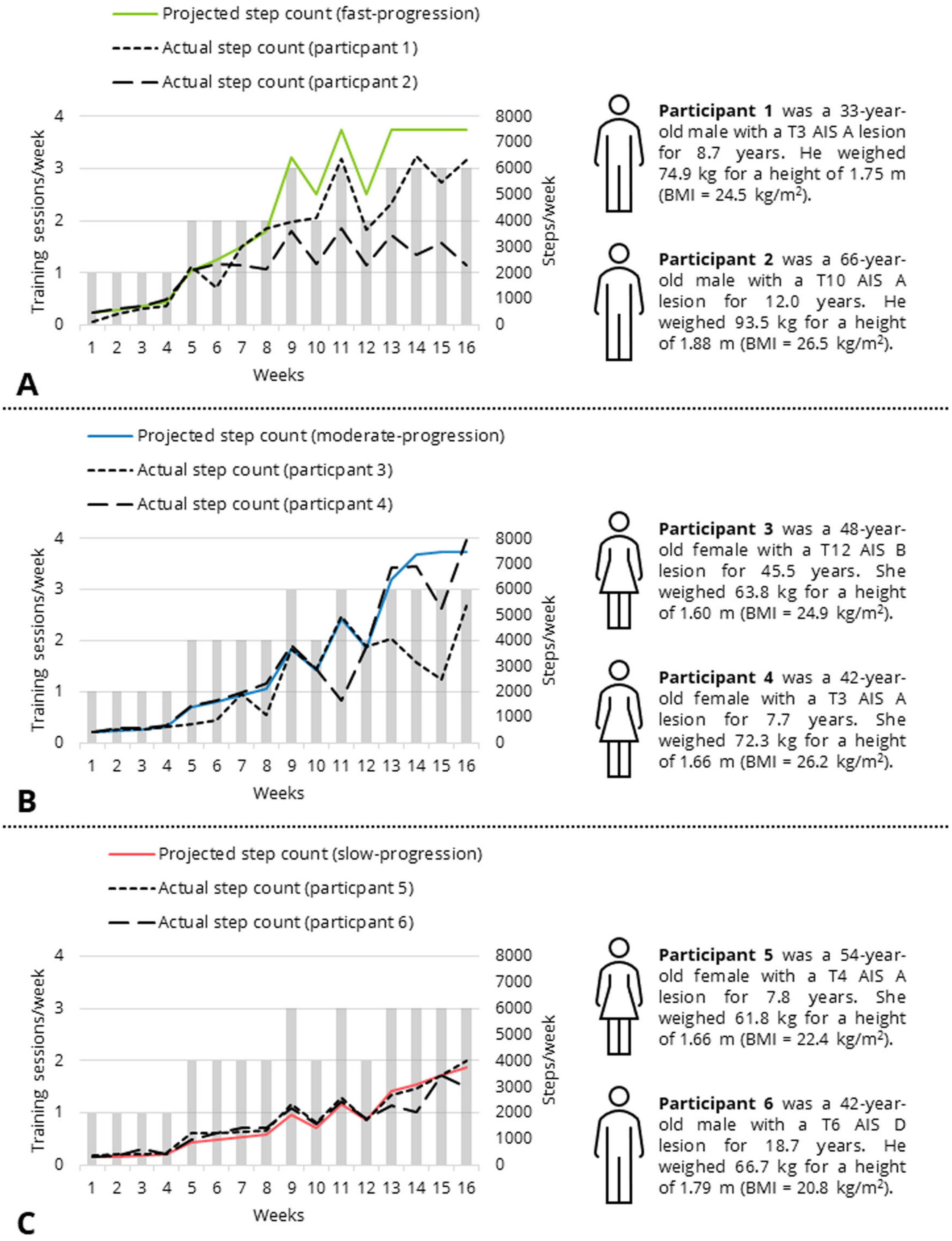
thereafter; individuals classified in the osteopenic profile are assigned to a moderate-progression program that begins with a session maximum of 400 steps during the first week and increases by up to 15% weekly thereafter; and individuals classified in the preserved bone mineral density profile are assigned to a fast-progression program that begins with a session maximum of 500 steps during the first week and increases by up to 20% weekly thereafter.

For all training volumes, the frequency of the (up to) 1 h training sessions increases from 1 to 3 times per week over an initial period of 16 weeks, fragmented into distinct phases. During the familiarization phase (weeks 1 to 4), 1 training session per week is recommended so that rehabilitation professionals can optimize exoskeleton adjustments and so that participants can safely learn the exoskeleton's functioning as well as proper walking technique. During the initial training phase (weeks 5 to 8), 2 training sessions per week are recommended and align with spinal cord injury exercise guidelines to improve cardiorespiratory fitness [10]. During the progression phase (weeks 9 to 12), oscillation between 2 and 3 training sessions per week are recommended to transition towards an increased participant tolerance and adaptation to higher training frequency (i.e., 3 training sessions/week). Finally, during the optimal training phase (weeks 13 to 16), 3 training sessions per week are recommended and align with spinal cord injury guidelines for optimal cardiometabolic health benefits [10]. This progression strategy, based on gradual monthly increases in "frequency" and "duration" (i.e., number of steps taken per session), is designed to limit peaks in training volume. Indeed, reported fractures during exoskeleton walking programs have been reported to occur during the first several training sessions (i.e., within the first five sessions) [2–4]. It is hypothesized that large increases in step number may surpass the tissues capability to adapt and increase fracture risk (further discussed hereunder) [2]. This progression strategy also aligns with the American College of Sports Medicine's recommendations for aerobic exercise [11].

This early-stage algorithm has been integrated into an active study to which participants provided free and informed consent [8]. Clinical characteristics of a heterogenous sample of 6 participants (male/female = 3/3) and their training data are presented in Fig. 2. From a clinical standpoint, all three training progression strategies prove to be feasible, particularly for participants with paraplegia, as most participants trained within their weekly targeted goals. Participant 2 plateaued at week 9 due to his body weight, as it excessively drained the exoskeleton batteries (Ekso GT, Ekso Bionics, Richmond, California, USA) and shortened his training sessions to about 30–35 min. However, for participant 3, physical fatigue predominantly inhibited her from reaching her weekly step targets during the optimal training phase. Importantly, no case of fracture has occurred thus far [8].

PROPELLING THE ALGORITHM TO THE NEXT STAGE

It is crucial to recognize that the current lack of empirical evidence impedes the development of an evidence-based algorithm for fracture-risk assessment and mitigation during exoskeleton-assisted walking programs. Hence, the World Health Organization's criteria for osteoporosis was used as a readily available way of characterizing bone strength and assigning individuals to one of the three modulated training progression strategies. However, this early-stage algorithm has limitations, some of which are discussed hereunder, that warrant further reflection and discussion among rehabilitation experts in an effort to refine it. As such, adoption and



Participant 1 was a 33-year-old male with a T3 AIS A lesion for 8.7 years. He weighed 74.9 kg for a height of 1.75 m (BMI = 24.5 kg/m^2).

Participant 2 was a 66-year-old male with a T10 AIS A lesion for 12.0 years. He weighed 93.5 kg for a height of 1.88 m (BMI = 26.5 kg/m^2).

Participant 3 was a 48-year-old female with a T12 AIS B lesion for 45.5 years. She weighed 63.8 kg for a height of 1.60 m (BMI = 24.9 kg/m^2).

Participant 4 was a 42-year-old female with a T3 AIS A lesion for 7.7 years. She weighed 72.3 kg for a height of 1.66 m (BMI = 26.2 kg/m^2).

Participant 5 was a 54-year-old female with a T4 AIS A lesion for 7.8 years. She weighed 61.8 kg for a height of 1.66 m (BMI = 22.4 kg/m^2).

Participant 6 was a 42-year-old male with a T6 AIS D lesion for 18.7 years. He weighed 66.7 kg for a height of 1.79 m (BMI = 20.8 kg/m^2).

Fig. 2 Projected versus actual step count data for the three distinct training progressions for participants ($n = 6$) enrolled into the walking program. **A** Projected step count (green) based on session maximums and participant data for the fast-progression program. Notice that a plateau in the number of steps/week is expected as of week 13. **B** Projected step count (blue) based on session maximums and participant data for moderate-progression program. Notice that a plateau in the number of steps/week is expected as of week 14. **C** Projected step count (pink) based on session maximums and participant data for slow-progression program. Notice that no plateau in the number of steps/week is expected during the 16-week period. AIS = American Spinal Injury Association (ASIA) Impairment Scale, BMI = Body Mass Index.

implementation of the proposed algorithm in clinical practice and research protocols remains premature at the present time. Additional scientific evidence gathered via robust qualitative or quantitative research protocols continues to be needed before doing so.

Is hip bone mineral density the best indicator of bone strength in this population?

Hip bone mineral density criteria were developed in the context of postmenopausal osteoporosis, which is associated with higher risks of hip fracture [9]. However, osteoporosis in individuals with spinal cord injury evolves differently, as bone loss in the lower limbs is greater distally (i.e., around the knee and ankle joints) and fragility fractures occur more often at the distal femur and proximal tibia, not at the hip [1]. Thus, combining bone mineral density at the hip to measurement obtained at other bone sites (e.g., distal femur, proximal tibia) has been recommended [5, 12]. Although fracture thresholds for bone mineral density in the knee region in men with chronic (i.e., ≥18 months) spinal cord injury have been reported previously (≤0.78 g/cm^2 measured with dual-energy X-ray absorptiometry), their use as a contra-indication to weight-bearing exercise is not currently recommended [5, 13]. Moreover, emerging modalities, such as peripheral quantitative computed tomography and quantitative ultrasound may also prove to be valuable in the evaluation and categorization of fracture risk in this population [5, 12]. However, recommending such alternate measurement tools may not be justified at the present time due to a lack of evidence [5].

Should other fracture-risk characteristics be integrated in this algorithm?

Solely assessing bone mineral density as a criterion for bone strength has been criticized as it fails to adequately identify people who previously sustain fragility fractures [9]. Thus, assessing additional risk factors may be crucial while refining this early-stage algorithm. Fracture-risk assessment algorithms incorporating additional risk factors have been implemented before. Probably the most widely recognized implementation of this is the Word Health Organization's Fracture Risk Assessment Tool (FRAX) [9]. This web-based tool considers age, sex, body mass index, personal and familial history of fragility fracture, smoking, glucocorticoid use, rheumatoid arthritis, secondary health conditions associated to osteoporosis, alcohol intake as well as femoral neck bone mineral density (optional). However, the need to develop a specific tool for spinal cord injury has been acknowledged since additional characteristics in this population are known to influence fracture risk (e.g., spinal cord injury duration, level and severity) [5, 12, 14]. To this effect, a tool to assess fracture risk based on commonly reported population-specific criteria has been previously proposed [12]. Using a 9-item checklist, authors suggest that the presence of three or more risk factors represents a moderate risk of fracture, while the presence of 5 or more risk factors represents a high risk of fracture. Unfortunately, to our knowledge, this tool has not been validated in the literature and it is currently unknown whether the proposed criteria correlate adequately with moderate and high risk of fracture, respectively. Nonetheless, this remains of high interest and may warrant further exploration through a broader scientific and clinical co-creation process.

Criteria for the diagnosis of sublesional osteoporosis in individuals with spinal cord injury that includes several population-specific risk factors, as well as unique bone mineral density criteria, have been proposed [12]. In males over the age of 60 and postmenopausal females, sublesional osteoporosis diagnosis is based on hip or knee region T-score ≤ −2.5 [12]. In males under 59 years and premenopausal females, sublesional osteoporosis diagnosis is based on hip or knee Z-score < −2.0 combined with the presence of at least 3 risk factors (age <16 years at injury, alcohol intake >5 servings/day, body mass index <19, spinal cord injury duration ≥10 years, female sex, motor complete lesion, paraplegia, family history of fragility fracture) [12]. Finally, for males or females of 16 years and older, a history of fragility fracture is considered sufficient to diagnose sublesional osteoporosis, regardless of age and menopausal status [12]. These diagnostic criteria could also be of interest to improve the early-stage algorithm presented in the current paper. For example, individuals who meet the proposed criteria for sublesional osteoporosis could be assigned to the slow-progression training program. Whereas individuals who have several risk factors (e.g., >2–3), but do not meet all criteria proposed for sublesional osteoporosis, could be assigned to the moderate-progression training program. Finally, individuals who have very few risk factors (e.g., ≤2–3) could be assigned to the fast-progression program. Again, further exploration through a broader scientific and clinical co-creation process is warranted.

Lastly, other factors may also warrant consideration when refining this early-stage algorithm. Notably, exoskeleton-specific attributes may have potential effects on lower-limb fracture risk and have been recently discussed elsewhere [2]. Likewise, whether or not an individual has successfully completed a locomotor training program, particularly an exoskeleton-assisted walking program, may also warrant consideration.

How should training volume progress?

This is another difficult question to answer. If volume progresses too slowly, the benefits of the walking program may be unnecessarily delayed, reduced, or absent. However, if volume progresses too quickly, the risk of fractures and other related secondary musculoskeletal impairments may be increased [2]. Hence, striking a balance becomes crucial to conciliate two imperatives: optimizing the potential intervention effects (e.g., beneficial bone adaptations) and preventing secondary musculoskeletal impairments (e.g., fragility fractures) during exoskeleton-assisted walking programs. While continuing to develop clinical experience, education, and skills (i.e., clinical expertise), strengthening current empirical evidence and documenting clients' perspectives remain of central importance to optimize the proposed preliminary algorithm. In fact, integrating clinical expertise, best research evidence and clients' perspectives are fundamental for evidenced-based practice when aiming to establish the most beneficial and safest starting point in terms of training volume and progression strategy during exoskeleton-assisted walking programs.

In individuals with chronic spinal cord injury, bone loss appears to be mainly due to continued inhibition of osteocyte-lead bone formation [15]. Osteocytes are sensitive to bone loading and respond by increased bone mineralization in areas of high load, thus changing bone architecture and increasing bone resistance (i.e., strength) against the initial stimulus [1]. As such, osteocytes may have a substantial effect on bone strength and fracture risk with relatively limited increases in total bone mineral density [1]. However, this process is slow, with measurable changes in bone strength only expected after a few months of training [1, 16]. Hence, if training progress too quickly, the load on the bone may surpass its adaptability and fracture may occur. Thus, volume progression must be adequately dosed to ensure that cumulative increases can be maintained over a medium-to-long-term period.

Training volume is defined here as the number of steps taken per week which are also subdivided by session. The algorithm proposes an approach for progressing volume over four distinct phases (familiarization, initial training, progression, optimal training). As illustrated in Fig. 2, volume does not increase linearly throughout the entire 16-week program. Firstly, there are steep increases in volume when transitioning between the familiarization, initial training and progression phases (i.e., between weeks 4 and 5, 8 and 9). This is mainly due to the additional training day per week that is added during these transitions. These steep increases in volume were anticipated and accepted to maintain participant motivation/satisfaction. Indeed, decreasing the number of steps per session during these transition periods to maintain a perfectly linear increase in volume could be discouraging for participants (may be interpreted as a regression in performance or ability). Secondly, training volume follows a "sawtooth" scheme during the progression phase (weeks 9 to 12) which is mainly due to the variation between 2 and 3 training sessions per week. This volume design was chosen to alleviate peaks in volume when transitioning from 2 to 3 sessions per week. This also helps ensure participant tolerance to three sessions per week. Finally, a plateau is noted for the moderate and fast-progression programs during the optimal training phase (weeks 13 to 16). This is predominantly due to the time/scheduling constraint imposed by the 1 h training session. Based on data gathered thus far, participants can optimally take about up to 2500 steps during 1 h sessions with the exoskeleton parameters providing maximal walking speed (i.e., on our exoskeleton this equates to ProStep/ProStep+ mode with swing time reduced to its minimum). This plateau was accepted as indefinite increase is not realistic nor necessarily desirable in the present context of use.

FINAL REMARKS

The presented early-stage algorithm calls for rehabilitation clinicians and scientists to engage in its refinement and serves to furhter increase awareness of lower-limb fracture risk during exoskeleton-assisted walking programs. Limited empirical evidence remains a major obstacle in developing an evidence-based algorithm and, even more so, adopting or implementing such an algorithm in clinical practice or research protocols. To this effect, it is essential that researchers serve as leaders in ensuring the safety of their participants based on scientific evidence, particularly given the rapid progress of robotic exoskeleton technologies and the challenges associated to their use in clinical practice.

REFERENCES

1. Clark JM, Findlay DM. Musculoskeletal health in the context of spinal cord injury. Curr Osteoporos Rep. 2017;15:433–42.
2. Bass A, Morin SN, Vermette M, Aubertin-Leheudre M, Gagnon DH. Incidental bilateral calcaneal fractures following overground walking with a wearable robotic exoskeleton in a wheelchair user with a chronic spinal cord injury: is zero risk possible? Osteoporos Int. 2020;31:1007–11.
3. Benson I, Hart K, Tussler D, van Middendorp JJ. Lower-limb exoskeletons for individuals with chronic spinal cord injury: findings from a feasibility study. Clin Rehabil. 2015;30:73–84.
4. van Herpen FHM, van Dijsseldonk RB, Rijken H, Keijsers NLW, Louwerens JWK, van Nes IJW. Case Report: Description of two fractures during the use of a powered exoskeleton. Spinal Cord Ser Cases. 2019;5:99.
5. Morse LR, Biering-Soerensen F, Carbone LD, Cervinka T, Cirnigliaro CM, Johnston TE, et al. Bone mineral density testing in spinal cord injury: the 2019 ISCD official positions. J Clin Densitom. 2019;22:554–66.
6. Esquenazi A, Talaty M, Packel A, Saulino M. The ReWalk powered exoskeleton to restore ambulatory function to individuals with thoracic-level motor-complete spinal cord injury. Am J Phys Med Rehabil. 2012;91:911–21.
7. Asselin PK, Avedissian M, Knezevic S, Kornfeld S, Spungen AM. Training Persons with Spinal Cord Injury to Ambulate Using a Powered Exoskeleton. J Vis Exp. 2016;112:e54071.
8. Bass A, Aubertin-Leheudre M, Vincent C, Karelis AD, Morin SN, McKerral M, et al. Effects of an overground walking program with a robotic exoskeleton on long-term manual wheelchair users with a chronic spinal cord injury: protocol for a self-controlled interventional study. JMIR Res Protoc. 2020;9:e19251.
9. Baim S, Leslie WD. Assessment of fracture risk. Curr Osteoporos Rep. 2012;10:28–41.
10. Martin Ginis KA, van der Scheer JW, Latimer-Cheung AE, Barrow A, Bourne C, Carruthers P, et al. Evidence-based scientific exercise guidelines for adults with spinal cord injury: an update and a new guideline. Spinal Cord. 2018;56:308.
11. American College of Sports MedicineLiguori G, Feito Y, Fountaine C, Roy BA. ACSM's guidelines for exercise testing and prescription. 11th ed. Philadelphia: Wolters Kluwer; 2022.
12. Craven Robertson, McGillivray Adachi. Detection and treatment of sublesional osteoporosis among patients with chronic spinal cord injury. topics in spinal cord injury. Rehabilitation. 2009;14:1–22.
13. Garland D, Adkins R, Stewart C. Fracture threshold and risk for osteoporosis and pathologic fractures in individuals with spinal cord injury. Top Spinal Cord Inj Rehabil. 2005;11:61–9.
14. Cervinka T, Lynch CL, Giangregorio L, Adachi JD, Papaioannou A, Thabane L, et al. Agreement between fragility fracture risk assessment algorithms as applied to adults with chronic spinal cord injury. Spinal Cord. 2017;55:985–93.
15. Tan CO, Battaglino RA, Morse LR. Spinal cord injury and osteoporosis: causes, mechanisms, and rehabilitation strategies. Int J Phys Med Rehabil. 2013;1:127.
16. Soleyman-Jahi S, Yousefian A, Maheronnaghsh R, Shokraneh F, Zadegan SA, Soltani A, et al. Evidence-based prevention and treatment of osteoporosis after spinal cord injury: a systematic review. Eur Spine J. 2018;27:1798–814.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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