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Anterior cruciate ligament reconstruction results in alterations in gait variability

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Abstract

Introduction: The temporal structure of gait variability has shown that healthy human gait exhibits long-range correlations and deterministic properties which allow the neuromuscular system to be flexible and adaptable to stresses. Pathology results in deterioration of these properties. We examined structure of gait variability after ACL reconstruction with either BPTB or quadrupled ST/G tendon autografts.

Methods: Six patients with BPTB reconstruction, six with ST/G reconstruction and six healthy controls walked on a treadmill at their self-selected pace. Two minutes of continuous kinematic data were recorded with a 6-camera optoelectronic system. The nonlinear measure of the largest Lyapunov Exponent (LyE) was estimated from the knee flexion-extension time series from 100 continuous walking strides to assess the structure of gait variability.

Results: The reconstructed limbs in both reconstructed groups exhibited significantly larger LyE values than the control limbs ($p < 0.05$), even though clinical outcomes indicated complete restoration. No significant differences were found between the two autografts. In addition, the intact contralateral leg produced significant higher LyE values as compared with the ACL-reconstructed leg in both groups. No interaction was found.

Discussion: The larger LyE values indicate that the reconstructed knees of both reconstructed groups exhibit more divergence in the movement trajectories during gait. The larger LyE values found in the intact leg in both reconstructed groups could be interpreted as a compensatory mechanism. However, the increased divergence found in both limbs may present an alternative explanation for the impaired neuromuscular performance and increased susceptibility to future pathology, which is supported by the increased amount of osteoarthritis found in ACL-reconstructed patients.

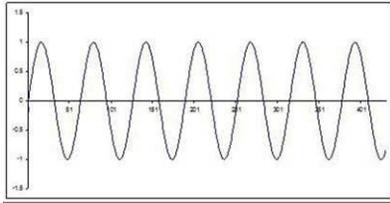
1. Introduction

It has been found that Anterior Cruciate Ligament (ACL) rupture affects gait variability [1–3]. The absence of the ACL signifies not only the loss of a mechanical restraint of the knee, but also the loss of afferent input due to the mechanoreceptors that exist in the ligament [4,5] thus affecting the function of the neuromuscular system [6]. However, it is unknown if an ACL reconstruction can restore these properties to normal physiological level [7–13].

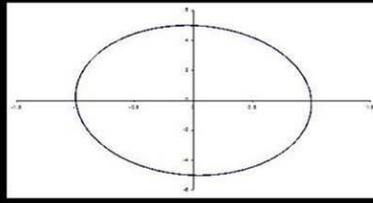
In addition, since an ACL reconstruction produces different functional outcomes (i.e., muscular activation patterns, proprioception) if it is performed using either a bone-patellar tendon-bone (BPTB) or a quadrupled hamstrings tendon (semitendinosus and gracilis; ST/G) autograft [7,9,10,12]. Biomechanical evaluations have demonstrated that differences do exist between the two autografts but they have not reached a consensus regarding the superiority of one autograft over the other in restoring neuromuscular function at the knee joint [10,12,13]. This is most evident in systematic reviews that have conflicting results as each favour one or the other graft [14]. It is possible that the examination of gait variability could better elucidate which autograft (BPTB or ST/G) is more suitable for ACL reconstruction.

Variability can be evaluated using traditional linear measures. However, they can only estimate the magnitude of variability at certain time occurrences, while the temporal evolution of movement patterns is ignored. In addition, gait kinematic parameters are extensively “treated” algorithmically (i.e., smoothing, differentiation, normalization) to provide with a “mean” picture of the subject’s movement distorting the temporal structure of variability [15]. On the contrary, measures from nonlinear dynamics estimate how a motor behaviour changes over time and provide information about the structure or organization of the movement [15,16].

In a previous study gait variability after ACL reconstruction was examined using the nonlinear parameter of Approximate Entropy (ApEn) which evaluates the regularity or predictability of a system [17]. It has been found that after ACL reconstruction using either BPTB or ST/G autografts the ACL-reconstructed knee exhibits greater ApEn values compared to a control knee. No difference was noted between the two reconstructed groups. However, in this study there was no data on the contralateral limb while it has been shown that after ACL reconstruction there are biomechanical adaptations in the intact knee as well [7,11]. On the other hand, Lyapunov Exponent (LyE) is a nonlinear measure that has been previously used in gait [1,2,18–23]. LyE estimates the underlying structure of variability during movement and it is particularly effective for movement data with inherent periodicity [15,21]. This measure has also been used in the study of postural control and the development of a new approach concerning neurologic physical therapy [24]. In addition, similar methodology has been applied for the investigation of the effect of walking speed and turning on gait properties of healthy individuals and it has been found that both conditions alter gait variability [22,23].

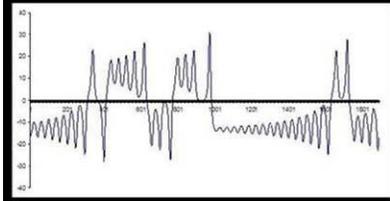


(a)

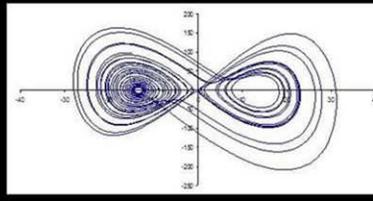


(b)

LyE=0.001

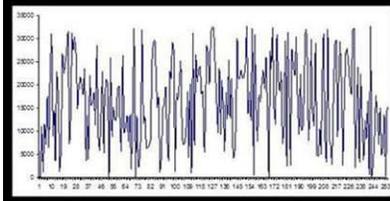


(c)

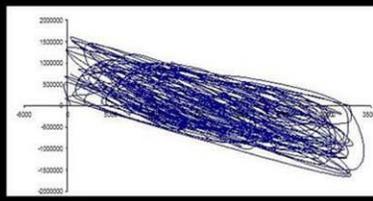


(d)

LyE=0.076

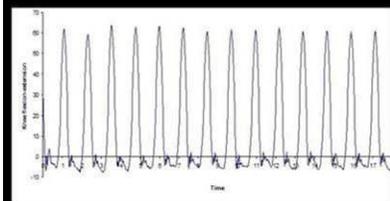


(e)

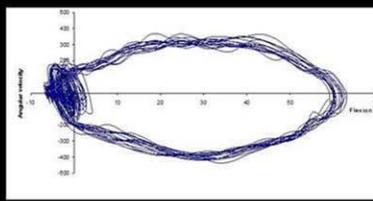


(f)

LyE=0.395

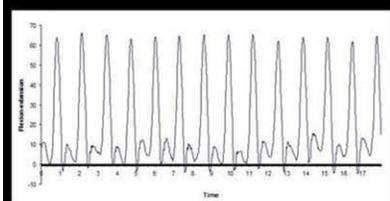


(g)

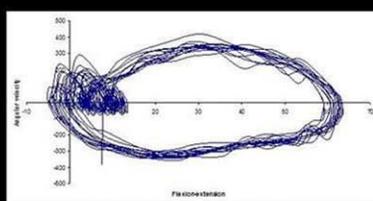


(h)

LyE=0.120

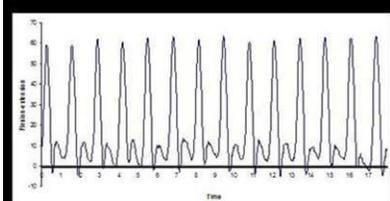


(i)

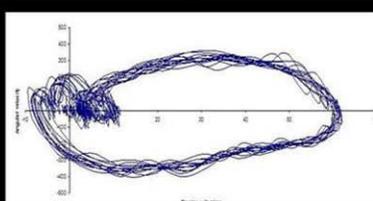


(j)

LyE=0.142

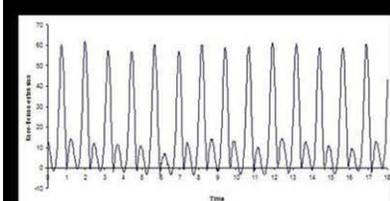


(k)

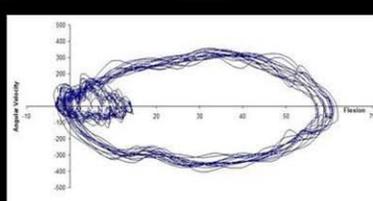


(l)

LyE=0.158

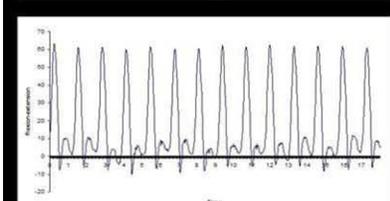


(m)

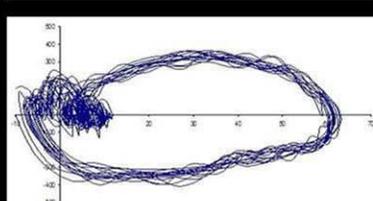


(n)

LyE=0.140



(o)



(p)

LyE=0.148

Fig. 1. Graphic representation of a periodic system [$\sin(1/10)$] (a), a chaotic system (the Lorenz attractor) (c), a random system (Gaussian noise centered on zero and a standard deviation of 1.0) (e), and of knee flexion-extension time series from a control (g), a BPTB reconstructed knee (i) and the intact contralateral knee (k) a ST/G reconstructed knee (m) and the contralateral intact knee (o). Their corresponding phase plane plots (b, d, f, h, j, l, n, and p), where the time series data is plotted versus the first derivative, are also provided. The LyE values for each time series are provided next to the correspondent state plots. Periodic systems are organized and are repeatable and predictable (a and b). Random systems, on the other hand, contain no order and are unpredictable. Their behaviour is never repeated (e and f).

In the present study we used the LyE to investigate the structure of gait variability after ACL reconstruction using either a BPTB or a quadrupled ST/G tendon autograft. We hypothesized that ACL reconstruction using either a BPTB or an ST/G autograft will affect the structure of gait variability as compared to healthy controls as well as to the healthy contralateral knee. In addition, if differences are identified between the two grafts, then the results of the present study may be able to elucidate the debate that exists in the sports medicine community with respect to the superiority of one graft over the other.

2. Materials and methods

Six male patients ACL-reconstructed with a BPTB autograft (age: 23 ± 2 years; mass: 83 ± 5 kg; height: 179 ± 5 cm), six male patients ACL-reconstructed with a ST/G autograft (age: 24 ± 3 years; mass: 78 ± 8 kg; height: 176 ± 7 cm) and six healthy control subjects who had never suffered of any kind of orthopaedic or neurological condition (age: 27 ± 3 years; mass: 80 ± 3 kg; height: 182 ± 5 cm) participated in the study. No statistical significant differences were found for age, mass or height among the three groups ($p = 0.17$, $p = 0.14$, $p = 0.16$, respectively). The patients were randomly assigned to the two groups (BPTB and ST/G). The time elapsed from ACL reconstruction was $25 (\pm 4.5)$ months for the ST/G patients and $21 (\pm 5.4)$ months for the BPTB reconstructed patients ($p = 0.18$). In all cases the diagnosis of complete ACL rupture was confirmed during the arthroscopic reconstruction. Patients with chondral lesions, posterior cruciate or collateral ligament injury, meniscal injuries in which a meniscectomy or a suture of the meniscus was performed, previous injury or other orthopaedic or neurological pathology were excluded from our study. All patients followed the same rehabilitation protocol. The study was approved by the Human Studies Committee of our Medical Center. All subjects provided informed consent according to the declaration of Helsinki prior to entering the study.

All patients were operated by the same orthopaedic surgeon (senior author, AG),

under general anesthesia, with a tourniquet placed as proximal as possible. After the preparation and marking of the graft insertion site on the femur and tibia, the autograft (quadrupled ST/G or BPTB) was harvested and prepared. The BPTB graft was harvested from the medial third of the patellar tendon [25]. The tibial tunnel was drilled at an angle of 60° to the plateau, with a diameter of 10 mm for BPTB autograft, or according to the autograft diameter for the ST/G (8–9 mm). The femoral tunnel was drilled through the anteromedial portal having the knee flexed in 120°. BPTB autografts were fixed with bio-absorbable interference screws (Bio-Rci, Smith & Nephew Endoscopy, Andover, MA, USA) on both the femoral and tibial side. ST/G autograft fixation was performed with an EndoButton (Smith & Nephew Endoscopy, Andover, MA, USA) at the femur and with a bio-absorbable interference screw at the tibia (Bio-Rci Smith & Nephew Endoscopy).

Clinical assessment was performed for all subjects by the same clinician using standard procedures. Static knee stability was evaluated with the manual Lachman test and the KT-1000 arthrometer (MEDmetric Corp., San Diego, CA, USA). The Lysholm score, the Tegner activity level and the International Knee Documentation Committee (IKDC 2000) score were also acquired to assess clinical outcome of the ACL reconstruction [26,27].

All subjects walked on a motorized treadmill (SportsArt 6005; SportsArt America; Woodinville, WA, USA), while a 6-camera system (Peak Performance Technologies, Inc., Englewood, CO, USA) captured the movements of fifteen reflective markers placed on selected bony landmarks of the lower limbs and the pelvis [28]. All markers were positioned on the participating subjects by the same examiner. Using anthropometric measurements and the position of the reflective markers, we calculated the three-dimensional knee joint angular displacement [28]. In the present study, we analyzed the sagittal knee angular displacement (flexion/extension) of the knee. We collected three-dimensional data instead of two-dimensional to minimize measurement error due to perspective error [29]. Once they had all the markers placed and prior to data acquisition, all subjects were given time to warm up and familiarize with walking on the motorized treadmill at their self-selected pace which represented their most comfortable and natural walking speed. The familiarization period was six minutes which is considered sufficient for the achievement of reliable measurements [30]. After the familiarization period, data were collected continuously for two minutes at 50 Hz (at least 100 continuous walking strides).

The structure of gait variability was estimated with the largest Lyapunov Exponent (LyE) for the knee flexion-extension time series [15,31] (Figs. 1 and 2). Joint kinematic variability was examined because it has been shown that variability of stride characteristics (i.e., stride time) offers a less sensitive measure of differences between groups than variability of the joint kinematics [32]. Each time series consisted of 6000 data-points which is considered sufficient for the computation of the LyE [15]. The data were analyzed unfiltered so as to get a more accurate representation of the variations within the system [33]. It was

assumed because the same instrumentation was used for all subjects, the level of measurement noise would be consistent for all subjects and thus differences could be attributed to changes within the system itself [15].

The LyE is a measure of the structure or organization of the variability present in a time series and is calculated as the divergence of the data trajectories in phase space, where the phase space is an n-dimensional space with n being large enough to unfold the attractor state [31]. The LyE describing purely sinusoidal data with no divergence in the data trajectories is zero because the trajectories overlap rather than diverge in phase space (Fig. 1). The LyE for random noise which has a lot of divergence in the data trajectories is relatively large (Fig. 1). The LyE for each joint time series and for each subject-condition was calculated using the Wolf et al. [34] algorithm implemented in the Chaos Data Analyzer (Professional Version, Physics Academic Software, Raleigh, NC, USA). More details for the calculation of the LyE are provided in the APPENDIX. For our calculations the number of embedded dimensions was 5.

Means and standard deviations were calculated for all three groups for the LyE. The mean values computed were submitted to a one-way analysis of variance (ANOVA). Post hoc differences were assessed using the Tukey test. In addition a two by two analysis of variance was performed to assess differences of the two groups and the contralateral intact knee. Therefore the between factor was identified as the reconstructed group (BPTP versus ST/G) and the within factor was identified as the leg (reconstructed knee versus intact contralateral). The level of significance was set at 0.05. The statistical analysis was performed using SPSS (Base 12.0, SPSS Inc., Chicago, IL, USA).

3. Results

Conventional methods indicated that ACL reconstruction fulfilled the intended goal. No differences were found between the BPTB and the ST/G reconstructed group for the Lysholm score (96 ± 3 and 95 ± 5 , respectively, $p = 0.35$). This was also the case for the IKDC subjective evaluation form (92 ± 7 for the BPTB group; 90 ± 10 for the ST/G group, $p = 0.4$). According to the IKDC objective evaluation two patients were graded as A and four as B in the BPTB group, while all the patients in the ST/G group were graded as B. In all cases side-to-side difference using the KT-1000 arthrometer was found to be “normal” (less than 5 mm). In addition, there were no differences between the pre-injury and post-operative Tegner scores in both groups, verifying that all patients had returned to their pre-injury activity level (7.1 and 6.7 for the BPTB group, $p = 0.21$; 7 and 6.7 for the ST/G group, $p = 0.22$). The mean Tegner score for the control group was 6.9 . No differences were found for the Tegner Score between the control group and the reconstructed groups ($p = 0.3$). The above results showed that the clinical outcomes of the conventional methods used for evaluation of both ACL-reconstructed groups have returned to normative levels.

However, the one-way ANOVA results showed significant differences in the LyE values ($F_{2,15} = 5.43$, $p = 0.016$) between the reconstructed knee and the healthy control knee (Fig. 3). The Tukey

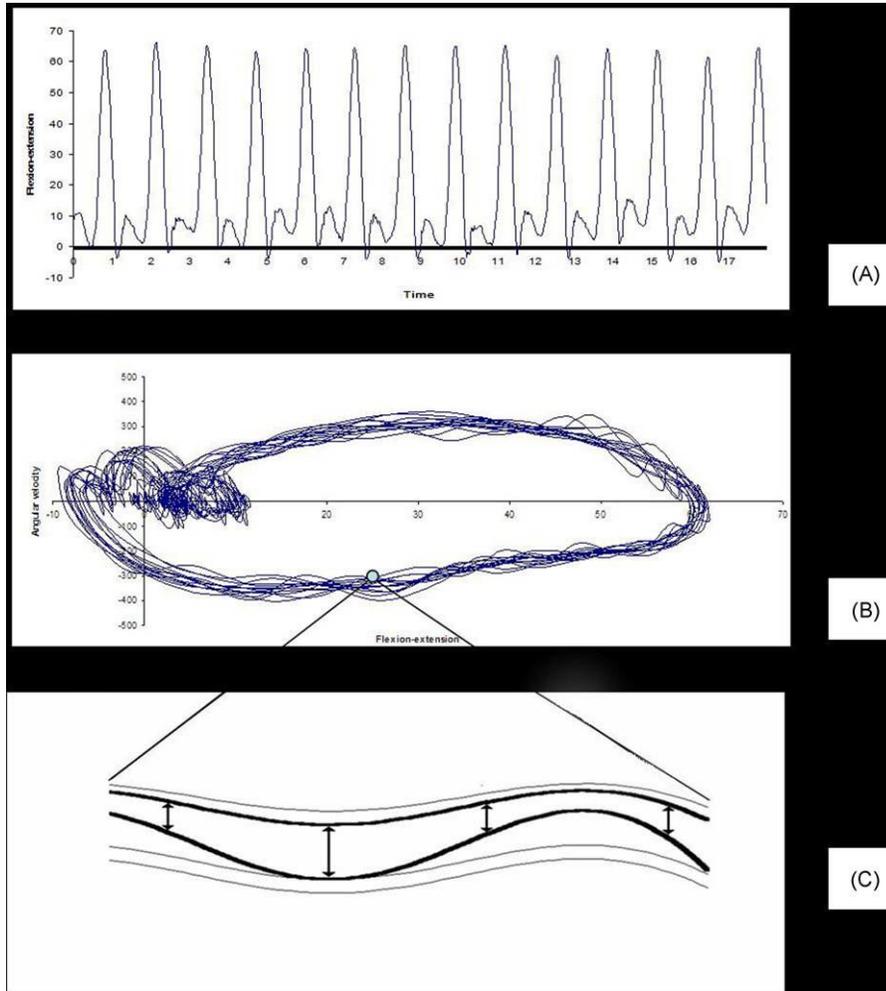


Fig. 2. A graphical representation of the state space and the calculation of the LyE.

(A) An original knee angle data set for several strides.

(B) A two-dimensional phase space is generated from this entire data set using every single point.

(C) A section of the phase space where the divergence of neighboring trajectories is outlined. The LyE is a measure of the rate at which nearby trajectories in phase space diverge. It should be noted that before calculating the LyE, we estimated the number of embedded dimension needed using the global false nearest neighbor (GFNN) analysis

[31]. The GFNN calculation revealed that five dimensions is required to reconstruct the phase space from a given time series. The estimation of the embedded dimensions value allowed the calculation of the LyE, which is a measure of the rate of divergence of the data trajectories in phase space, where the phase space is an n -dimensional space with n being large enough to unfold the attractor state.

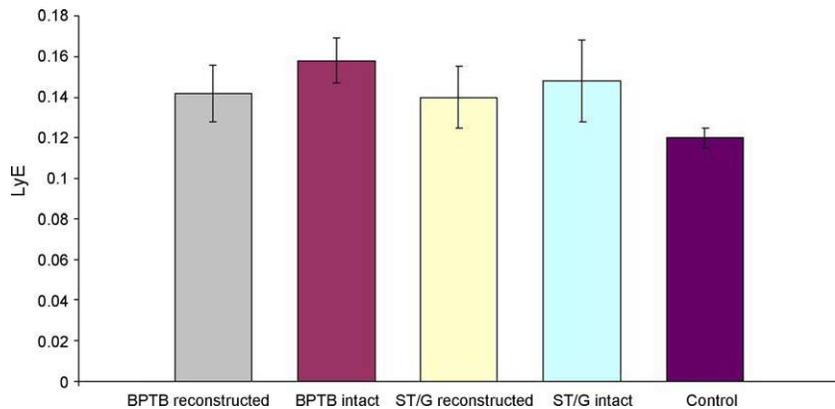


Fig. 3. Bargraph indicating the means and the standard deviations of the LyE values for all groups. Significant differences were found between the healthy control group and both ACL-reconstructed groups and between both ACL-reconstructed legs and their intact contralateral. No differences were found between the two ACL-reconstructed groups using either a bone-patellar tendon-bone (BPTB) or a quadrupled hamstrings tendon (semitendinosus and gracilis; ST/G) autograft

post hoc analysis revealed no significant differences between the BPTB and the ST/G LyE values ($p = 0.432$). However, the BPTB group had significantly larger LyE values (0.142 ± 0.014) than the healthy control (0.120 ± 0.005 , $p = 0.007$). This was also the case for the ST/G group (0.140 ± 0.015) which also showed significantly larger LyE values as compared to the healthy control ($p = 0.012$). The statistical power of our analysis was found to be 75.7% as calculated according to Cohen [35].

The results of the 2X2 ANOVA revealed a significant main effect for the leg factor ($F_{1,10} = 8.82$, $p = 0.014$; Fig. 3). Specifically, the intact contralateral leg produced significantly higher LyE values as compared with the ACL-reconstructed leg in both groups (mean LyE value for the contralateral intact leg in the BPTB reconstructed group 0.158 ± 0.011 , mean LyE value for the contralateral intact leg in the ST/G reconstructed group 0.148 ± 0.02). No significant differences were found between the groups ($F_{1,10} = 0.54$, $p = 0.47$) as expected based on our one-way ANOVA results presented above. In addition, no significant interactions were found between the two factors ($F = 1.276$, $p = 0.285$).

The mean self-selected speed for the BPTB group was $0.86 (\pm 0.11)$ meters per second, for the ST/G group was $0.90 (\pm 0.09)$ meters per second, and for the control group was $0.91 (\pm 0.12)$ meters per second. No significant differences ($p = 0.570$) were found between groups regarding their speed, and thus this variable was excluded as a possible confounder of our gait variability results.

4. Discussion

We examined the effect of an ACL reconstruction using BPTB and quadrupled ST/G tendon autografts on the structure of gait variability. We evaluated how knee flexion-extension changes over multiple strides during walking using the nonlinear measure of the largest Lyapunov Exponent (LyE). We hypothesized that ACL reconstruction using either a BPTB or a ST/G autograft would affect the structure of gait variability as compared to healthy controls as well as the healthy contralateral knee. In addition, if differences were found between the two grafts, then the results of the present study could elucidate the debate that exists in the sports medicine community with respect to the superiority of one graft over the other.

Our results showed that both the BPTB reconstructed group and the ST/G reconstructed group exhibit significantly larger LyE values than the control group. This result supports our first hypothesis. As suggested in the literature, this result could be related to the altered muscle activity found in the ACL-reconstructed knee. Specifically, Hiemstra et al. [7] demonstrated that there is both a knee extensor and knee flexor strength deficit and that there are also changes in neuromuscular balance [8] in the ACL-reconstructed knee using hamstrings autograft when compared to a control knee. Moreover, several authors have illustrated that ACL reconstruction with the ST/G graft results in knee extensor, knee flexor and tibial internal rotation deficits [9,10,13]. In addition, it has been shown that BPTB reconstructed knees exhibit an increased quadriceps strength deficit while the ST/G reconstructed knees have an increased hamstrings strength deficit [11]. These alterations in muscle performance could be neural or mechanical in origin. Specifically, the lack of proprioceptive activity deriving from the ruptured ligament or graft harvest site may alter neural control of the muscles around the knee [4,5]. Moreover, due to the different mechanics in the joint the afferent input from the mechanoreceptors around the knee joint may be different from those of a healthy knee.

The LyE values were also found to be larger in the contralateral intact knee as compared with the ACL-reconstructed in both groups. Thus, ACL reconstruction also affected the structure of gait variability in the intact contralateral leg. We believe that this result is a compensatory mechanism in order to maintain some degree of symmetry between the two legs. This is consistent with previous studies that have identified bilateral lower extremity accommodations in gait biomechanics and muscular performance in ACL-reconstructed patient [7,11]. Specifically, Hiemstra et al. [7] showed that there are strength deficits in the knee extensors and knee flexors also in the intact limb after ACL reconstruction, when compared to uninjured control group.

Furthermore, our results did not support a superiority of one graft over the other with respect to the structure of gait variability. No significant differences were found between the BPTB and the ST/G LyE values. This could signify that despite the different effects of each graft on muscle activity around the knee [8,9,10,13], the resultant outcome as measured through the structure of gait variability is the same.

The significance of the functional differences found in our study can be addressed through the optimality of variability proposition developed by Stergiou et al. [24]. According to this proposition, health is directly associated with an optimal state of the structure of variability. Decrease or loss of this optimal state of variability makes the system more rigid while increase beyond this optimal level makes the system more noisy and unstable. Both situations render the system less adaptable to perturbations and environmental demands and are directly associated with lack of health. Interestingly, while ACL reconstruction is associated with greater values of LyE in gait variability, ACL deficiency is related to smaller values of LyE in gait variability [2]. Thus, the ACL deficient knee may be more rigid in its neuromuscular behaviour, while the ACL-reconstructed knee exhibits greater divergence in its movement trajectory. Hence, ACL reconstruction did not restore optimal gait variability but, on the contrary, led to altered variability. It is possible that this behaviour by the ACL-reconstructed individuals is due to the absence of the proper neural feedback mechanisms via proprioception although mechanical stability has been restored as it was revealed by the clinical tests. Thus, according to the optimality of movement variability proposition, it could be speculated that the ACL-reconstructed knee is susceptible to injury and the development of future pathology. Indeed, long follow up studies have demonstrated the development of osteoarthritis in the ACL-reconstructed knee [36]. However, further studies are required to establish the relationship between altered structure of gait variability and increased incidence of injury or development of osteoarthritis.

Our results also indicated that the LyE measure could prove to be an important tool for the evaluation of various conditions that affect the neuromusculoskeletal system, which is consistent with other research [21–24,37]. Thus, we believe that the examination of the structure of variability in gait patterns using the LyE measure can eventually become a routine examination among orthopaedic surgeons to examine the functional outcome of an ACL reconstruction, or any disorder that affects gait.

There are certain limitations of the study. Our subjects walked on a motorized treadmill instead of overground. However, Matsas et al. [30] and Chang et al. [38] demonstrated that knee joint kinematics and stride dynamics from familiarized treadmill walking can be generalized to overground walking. Furthermore, the collection of a large number of continuous data required for the evaluation of gait variability and the necessity to make certain the walking speed remains constant for each condition enforce the walking measurements to be collected on a motorized treadmill. Walking overground is not typically associated with a constant speed for a long period of time (such as in the case with multiple footfalls) as a result of intermittency [39,40]. Speed can affect variability during walking [22]. Therefore, by using a motorized treadmill, any confounding effects of the walking speed within conditions is eliminated. In addition, all three groups walked on the treadmill with statistically similar speeds. Also, the walking speed of the people participating in our study was smaller as compared to those reported in the literature. This could be due to the use of a treadmill. However, since all subjects walked on the same treadmill

and no difference was found between the two groups with respect to the walking speed, the validity of our results is not at risk. Another possible limitation is the small number of patients that formed the two ACL-reconstructed groups. However, the statistical power was found to be 75.7% which supports our results [35]. Nonetheless, larger numbers are necessary to confirm these findings. In addition, females and older people need to be studied to extend our findings to these groups. Finally, in our study the algorithm developed by Wolf et al. [34] was used, which has been shown to be sensitive to noise in small data sets. There are other algorithms available, such as the Rosenstein et al. [41], however, the superiority of one algorithm over the other for physiological data sets have not been clearly established [42].

In conclusion, we evaluated the functional outcome of ACL reconstruction using either BPTB or ST/G graft two years after ACL reconstruction. Functional evaluation was done through the examination of the structure of variability in the knee flexion-extension movement patterns during gait using the nonlinear measure of LyE. Our results showed that both the BPTB reconstructed group and the ST/G reconstructed group exhibit significantly larger LyE values than the healthy control. In addition no difference was found between the two grafts which indicates a lack of superiority of one graft over the other with respect to gait variability. According to the optimality of variability proposition the altered structure of gait variability could signify increased susceptibility to injury and future pathology. However, additional studies are required to establish this result and elucidate its potential predictive significance. Furthermore, our results could suggest that post-surgical rehabilitation programs should be developed that focus on various neuromuscular control and balance exercise that may directly address the increased kinematic variability identified in our study for the reconstructed groups.

Acknowledgments

The authors gratefully acknowledge the funding support from the General Secretariat for Research and Technology of the Ministry of Development, as well as the European Social Fund of E.U. Dr Nicholas Stergiou is also supported by the NIH/NCMRR (K25HD047194) and the Nebraska Research Initiative. Conflict of interest The authors declare that there is no conflict of interest. Appendix A The usage of the LyE measure is based on examining the structural characteristics of the investigated data set that is embedded in an appropriately constructed state space. An appropriate state space is a vector space where the dynamical system can be defined at any point in time [31]. To properly reconstruct a state space, it is essential to quantify an appropriate time delay and embedding dimension for the investigated data set. Investigation of the characteristics of the state space is a powerful tool for examining a dynamic system because it provides information that is not apparent by just observing the data [31]. To reconstruct the state space, a state vector is created from the data set. This vector is composed of mutually exclusive information about the dynamics of the system (Eq. (1)).

$$\mathbf{y}(t) = [x(t), x(t - T_1), x(t - T_2), \dots] \quad (1)$$

where $\mathbf{y}(t)$ is the reconstructed state vector, $x(t)$ is the original data and $x(t - T_i)$ is time delay copies of $x(t)$. The time delay (T_i) for creating the state vector is determined by estimating when information about the state of the dynamic system at $x(t)$ is different from the information contained in its time-delayed copy.

If the time delay is too small then no additional information about the dynamics of the system would be contained in the state vector. Conversely, if the time delay is too large then information about the dynamics of the system may be lost and can result in random information. Selection of the appropriate time delay is performed by using an average mutual information algorithm (1) (Eq. (2))

$$I_{x(t),x(t+T)} = \sum P(x(t),x(t+T)) \log_2 \left[\frac{P(x(t),x(t+T))}{P(x(t))P(x(t+T))} \right] \quad (2)$$

where T is the time delay, $x(t)$ is the original data, $x(t+T)$ is the time delay data, $P(x(t), x(t+T))$ is the joint probability for measurement of $x(t)$ and $x(t+T)$, $P(x(t))$ is the probability for measurement of $x(t)$, $P(x(t+T))$ is the probability for measurement of $x(t+T)$. The probabilities are constructed from the frequency of $x(t)$ occurring in the time series. Average mutual information is iteratively calculated for various time delays and the selected time delay is at the first local minimum of the iterative process. This selection is based on previous investigations that have determined that the time delay at the first local minimum contains sufficient information about the dynamics of the system to reconstruct the state vector [31]. It is additionally necessary to determine the number of embedding dimensions to unfold the dynamics of the system in an appropriate state space. An inappropriate number of embedding dimensions may result in a projection of the dynamics of the system that has orbital crossings in the state space that are due to false neighbors and not the actual dynamics of the system [31]. To unfold the state space we systematically inspect $x(t)$ and its neighbors in various dimensions (e.g., dimension = 1, 2, 3,...etc.). The appropriate embedding dimension occurs when neighbors of the $x(t)$ stop being un-projected by the addition of further dimensions of the state vector (Eq. (3)).

$$y(t) = [x(t), x(t+T), x(t+2T), \dots, x(t+(d_E-1)T)] \quad (3)$$

where d_E is number of embedding dimensions, $y(t)$ is the d_E -dimensional state vector, $x(t)$ is the original data, and T is the time delay. A global false nearest neighbors algorithm with the time delay determined from the local minimum of the average mutual information is used to determine the number of necessary embedding dimensions to reconstruct the step time interval data series [31]. The calculated embedding dimension indicates the number of governing equations that are necessary to appropriately reconstruct the dynamics of the system [31]. The Tools for Dynamics (Applied Chaos LLC, Randle Inc., San Diego, CA, USA) software was used to calculate the embedding dimension for our data sets, and it was found to be five.

Subsequently, the LyE is calculated using the Wolf et al. [34] algorithm implemented in the Chaos Data Analyzer (Professional Version, Physics Academic Software, Raleigh, NC, USA). Briefly this algorithm is as follows:

- 1) Let $x(t)$ be a scalar time series with length N , where $t = 1, 2, \dots, N$. Select the embedding dimension (m) and time lag (t) for time delay embedding reconstruction as described above.
- 2) Randomly select an embedded point as an initial condition. This embedded point is a delay vector which has m elements, $(x(t), x(t+t), \dots, x(t+(m-1)t))$, and also this vector generates the reference trajectory.

- 3) Select its nearest neighboring vector, $(x(t_0), x(t_0 + t), \dots, x(t_0 + (m-1) \cdot t))$ on another trajectory.
- 4) Let the distance between these two vectors be $L(t_0)$ and $L'(t_1)$ after time evolution of t_1 .
- 5) Look for a new vector [34].
- 6) Let $L(t_1)$ be the length between a new vector and the evolved vector on the reference trajectory. The new vector must be selected so that $L(t_1)$ is small. The angular separation between the new vector and evolved vector on the reference trajectory must be small.
- 7) Repeat this procedure until the reference trajectory has gone over the entire data set.
- 8) Calculate the largest LyE by

$$\lambda_1 = \frac{1}{t_M - t_0} \sum_{k=1}^M \log_2 \frac{L'(t_k)}{L(t_{k-1})} \quad (4)$$

where M is the total number of replacement steps.

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