

Neck Motion Restriction Negatively Affects Turning Stability in Community-Dwelling Older Adults with and without a History of Falls

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Abstract

Background: Many older adults fall while turning. During the turning maneuver, rotation of the head precedes the rest of the body, creating a spatial frame of reference. Limitations of the neck rotation, may interfere with the turning mechanism, affect stability, and lead to recurrent falls. However, the association between the range of the neck rotation and turning stability was not explored yet. **Purpose:** To compare the impact of restricting the neck rotation by a brace, on the turning stability of adults with and without a history of falls. **Methods:** An observational, cross-sectional study consisting of 59 adults (average age 76 ± 6.9). A group ($N = 29$) with at least 2 falls (FL) in the last year and a group ($N = 30$) without a history of falls in the last year (NFL). All participants performed three tests: Timed up and Go (TUG), 180° Turn Test (180 TT) and 360° Turn Test (360 TT) with and without a neck brace. **Results:** All the scores of the FL were lower than those of the NFL ($p < 0.01$). Application of the brace worsened the performance of the 180 TT and the 360 TT of both groups ($p < 0.05$) but there was no interaction between group and bracing. The TUG score of only the NFL was affected by the brace ($p < 0.004$). Interestingly, only the range of the right neck rotation was correlated with balance tests and number of falls ($r = 0.272$; $p < 0.05$). **Conclusions:** Restricting of the neck mobility worsened the turning stability of both groups but without interaction. The study reinforces the need of considering the neck range of motion when addressing adult stability. A decrease in the range of right neck rotation was identified as a risk factor for loss of balance.

Keywords

Balance, Turning, Neck-Brace, Neck-Rotation, Fall

1. Introduction

Daily walking includes turning maneuvers, which comprise approximately 45% of all steps taken in a typical day [1]. Turning challenges stability and elicits specific balance strategies such as slowing down [2] and adding steps [3] [4]. The turning activity may become more demanding with aging, secondary to deterioration of sensory and motor function, reduced balance and increased falling accidents with all its adverse consequences [5] [6].

Turning is initiated by head rotation, followed by a cranio-caudal rotatory sequence, of the trunk and lower extremities [7]. Several studies have hypothesized that the initial head movement mainly provides visual surveying input [8] [9]. However as long as a similar movement pattern was detected during blinded turning, it is feasible that the rotation of the head provides sufficient information for aligning the body with the anticipated path of progression [10] [11] [12]. Interestingly, a systematic literature review revealed that the movement of the head while turning is of greater orientational importance than its final position [13].

The vestibular inputs have been found to play an important role in maintaining dynamic stability [14]. However, the input provided by the vestibular system is not sufficient to differentiate between the rotation of the head and the rest of the body during turning and additional proprioceptive information from the neck's muscles and joints are required. Moreover, active movements of the neck and stimulation of the neck's muscles by vibration, facilitate the activity of the vestibular system and assist to fine-tune it to the balancing requirements [13].

Holland *et al.* studied the effect of head immobilization on turning coordination [15]. They observed significant changes in the timing and amplitude of the trunk rotation when the head was immobilized, suggesting that proactive head realignment provides an egocentric reference for the body reorientation. Paquette *et al.* have illustrated that when older adults rotate their neck while walking they limit the amplitude and velocity of their neck rotation, for enhancing turning stability [16]. A similar stabilization strategy was advanced by a more recent cohort study, which revealed that adults who did not fall during a follow-up year demonstrated greater range of the head-on-shoulders rotation during a 360° turning test, than those who fell more than twice [17]. The researchers concluded that a head fixation might serve as a compensatory balance strategy that may lead to chronic neck stiffness and subsequent proprioceptive impairment.

Despite the demonstrated association of the head and neck mobility with the turning performance, their effect on turning equilibrium has barely been studied. Exploring of the impact of limiting neck mobility on the total body stabili-

ty, during various turning tests may provide important information for improving assessment and treatment of balance disorder.

The primary purpose of this study was to determine whether restricting neck rotation of adults with and without prior fall incidences, affects stability of the 180° Turn Test (180 TT), the 360° Turn Test (360 TT) and the Timed Up & Go test (TUG). The secondary goal was to examine whether the restriction affected differently the turning balance of older adults with and without a falling history.

The hypotheses were that limiting of the neck rotation would affect turning stability of both groups but would have a greater effect on adults with a history of falls. The rationale behind the hypotheses is that limiting of the neck rotation will reduce proprioceptive input and the additional hindrance to the already deteriorated motor control system of the fallers will exacerbate the proprioceptive deficit [17], freezing reaction [18], and the subsequent balance impairment below the critical threshold needed for effective motor performance [9] [13].

2. Methods

2.1. Setting and Study Participants

A convenience sample of 59 adults (10 men and 49 women, mean age 76 (± 6.9) years, range 65 - 91 years) was recruited. The inclusion criteria were 65 years of age or older and ability to ambulate independently without any assistive device a distance of at least 10 meters. The exclusion criteria were, acute cardiopulmonary conditions, neurological pathologies (stroke, multiple sclerosis, Parkinson's disease), acute vertigo, acute low back or cervical pain, cervical spine fusion, lower limb joint inflammation or amputation, and only a single fall in the previous year.

All participants signed an informed consent form. Demographics, general health, falling history, and level of physical activity data were collected from questionnaires and medical records. The first section of the Godin Leisure-Time Exercise Questionnaire was used to obtain the level of physical activity [19]. According to the responses in the questionnaire, about their falling history, the participants were divided into two groups: "A group of participants who fell" (FL) twice or more in the previous year ($N = 29$) and "A group with no reported fall" (NFL) in the previous year ($N = 30$) (**Table 1**). In order of facilitating memorization of the falls event and to verify their number, questions were asked regarding the nature, time, location of the falls and the subsequent treatment.

Baseline, range of motion of cervical rotation was measured, using a universal goniometer. The measurements were performed with subjects seated upright on a chair, supported by a backrest at the thorax level. A standard frame of eyeglasses was fitted with a midpoint mark, above the nasal bridge, serving as a point of reference for the goniometer's arm that accompanied the rotation of the head. The other arm remained stationary, facing forward. The measurements were found to have high intertester reliability for assessing left and right neck rotation ($ICC = 0.88; 0.86$, respectively) [20]. The validity of the technique was substantiated

Table 1. Background information of the participants.

Variable	All participants N = 59	FL ^a N = 29	NFL ^a N = 30	p-value Statistical Test
Age (years) (Mean ± SD)	76 (±6.9)	78.3 (±7.5)	73.9 (±5.7)	p = 0.13 t ₍₅₇₎ = -2.561
Gender (female) N (%)	49 (83.1%)	27 (93.1%)	22 (73.3%)	p = 0.08 Fisher's exact
BMI (Mean ± SD)	26.0 (±4.5)	25.9 (±3.4)	26.1 (±5.5)	p = 0.856 t ₍₄₉₎ = 0.182
Physical Activity Score ^b (Mean ± SD)	11.7 (±9.7)	10.3 (±9.8)	12.9 (±9.5)	p = 0.307 t ₍₅₇₎ = 1.03
Walking aids N (%)	12 (21.1%)	10 (35.7%)	2 (6.9%)	p = 0.01** X ² ₍₁₎ = 7.118
Number of ailments (Mean ± SD)	3.2 (±2.0)	3.8 (±2.0)	2.7 (±1.8)	p = 0.035* t ₍₅₇₎ = -2.161
Number of medications (Mean ± SD)	4.1 (±3.5)	5.3 (±4.2)	3.0 (±2.0)	p = 0.009** t ₍₄₀₎ = -2.740
Right Cx Rot ^c (Mean ± SD)	54.6 (±9.2)	51.9 (±8.7)	57.2 (±9.1)	p = 0.026* t ₍₅₇₎ = 2.285
Left	55.7 (±9.4)	53.7 (±8.8)	57.8 (±9.7)	p = 0.094 t ₍₅₇₎ = 1.701

Note: N, Number; FL, Fallers; NFL, Non fallers; SD, standard deviation; Cx Rot, Cervical spine rotation. ^aFL-Fell twice or more during the past year; NFL-No reported falls during past year. ^bScore for total weekly physical activity is calculated by the equation (light activity X 3) + (moderate activity X 5) + (strenuous activity X 9). ^cCervical spine rotation in degrees. *p < 0.05; **p < 0.01.

by correlating the measurements of the gold standard, Cervical Range of Motion tool and the current measurements ($r = 0.890$; 0.759 , to the right and left, respectively).

All subjects underwent three standard clinical balance tests: TUG [21], 180 TT [22] and 360 TT [23] [24], which are often used for detecting falling susceptibility in older people [23] [25] [26]. Each participant performed the TUG and 360 TT four times while being videotaped (Canon Powershot A2200), with and without an adjusted neck brace, which restricted the neck's rotation. Half of the participants in each group were randomly selected for taking the braced test, first. The camera was mounted on a tripod and filming was conducted from the side, perpendicular to the sagittal plane of the participants, at a distance that allowed recording from the waist down.

In order of analyzing and categorizing the 360 TT and the 180 TT, the video clips were separately scrutinized by two experienced physical therapists (with more than 10 years of practice, each). The 180 TT was partitioned from the TUG

test and was confined by the beginning and end of the turning path reversal. The last heel-strike prior to initiation of the reversal was denoted as the beginning of the turn, while the heel-strike of the first step back toward the chair was denoted as the completion of the turn (**Figure 1**). The examined parameters of the 180 TT were gradation of staggering, number of steps, time to accomplish a turn and turning strategy [22]. The scores of each section of the 180 TT ranged from 0 - 2, inversely proportional to the quality of the performance. To perform the 360 TT the participants were asked to turn around in place while the turning duration and the number of steps have constituted the recorded parameters. The research was conducted at the gym of the physical therapy clinic and each session lasted for about 1 hour. The total period of data collection lasted 2 months.

Each examiner separately screened all video clips, using the slow-motion and stop-action functions of the video system with an accuracy of one millisecond (Media Player Classic-Home Cinema version 1.7.10). To prevent bias, examinees were given a code name. After the analysis of the clips, the data of the two testers was compared. Any discrepancy was resolved by a conjoint decision.

The study was approved by the Ethics Committee of Clalit Health Services (0131-17-COM2).

2.2. Sample Size Estimation

The sample size was calculated based on duration and number of steps during 180 TT of adults with and without turning difficulty [22]. Calculation by G * Power for ANOVA: Repeated measures within-between interaction for a α error probability of 0.05, Power of 0.8 and a medium size effect of 0.25 revealed that 17 participants would be required for each group. However, considering that the reference study did not address the impact of the neck restriction on turning stability, the number of the participants in each group was increased to 30.

3. Data and Statistical Analysis

A descriptive analysis of group characteristics for nominal variables was presented by frequencies or percentage and was compared within the groups by chi-square or the Fisher's exact test. Continuous variables were presented by the



Figure 1. Specifying the initiation and the end of the turn during the TUG test. The last heel strike prior to the turn (a). The first heel strike after the completion of the turn (b).

mean values and standard deviations and were compared by t-Tests. Interaction of the brace effect and the stability status (fallers & non-fallers) was calculated by Two Way ANOVA. Spearman's Correlation was applied for estimating the relationship between the various variables. The odds Ratio of falling due to limitations in the range of neck rotation (RNR) was calculated using logistic regression. The significance level for all statistical tests was determined as $p < 0.05$. All the statistical analyses were performed using Statistical Package for the Social Sciences software (IBM SPSS Statistics version 23).

4. Results

The participants of the FL were older, more of them used walking aids, suffered more ailments, and took more medications (**Table 1**). Their average number of falls per year was 2.7 ± 1.1 (maximum = 4). The mean range of right RNR of the NFL was significantly higher ($p < 0.05$, 51.9 ± 8.7 (FL) and 57.2 ± 9.1 (NFL)).

All participants performed the three balance assessment tests with a neck brace (WB) and without a brace (WOB). Only 52 participants were included in the data analysis of 360 TT, because unnotably, seven individuals changed their turning direction between trials. A moderate to high correlation was found between the TUG scores and the turning scores of 180 TT and 360 TT ($r = 0.698$, 0.903 ; $p < 0.01$, respectively).

It was found that the 180 TT scores of the FL were lower than the NFL ($p < 0.01$) and that limiting of the neck movement by a brace worsens the 180 TT scores of the FLs and NFLs as well (**Table 2**). In the 360 TT, alike the 180 TT, a significant difference was found between the FL and the NFL groups and within each group (WB Vs WOB) (**Table 2**).

At both testing conditions, the mean TUG score of the FL was significantly higher ($p < 0.01$) than that of NFL (WOB 18.5 ± 7.4 vs. 10.7 ± 2.8 and WB 19.3 ± 7.3 vs. 11.7 ± 3.7 , respectively) (**Table 2**). However, interestingly, wearing of the brace increased the TUG score of only the NFL group ($p < 0.01$).

For all balance tests, there were no significant interactions between group and neck restriction. Implying, that bracing did not exacerbate the balance disorder of the FL to a higher extent than that of the NFL. However, it is worth noting that in all balance tests with the neck brace the stability score of the FL was worse than of the NFL.

The age group with the highest prevalence was 70 - 79.9 years (27 subjects, 45.8% of all subjects) with an average left and right rotation range of 54.7 and 57.6, respectively. The age group of above 90 constituted 3.4% of all subjects (2 participants) and demonstrated the lowest average right neck rotation. Age was significantly correlated only with right RNR ($r = 0.269$; $p < 0.05$) (**Table 3**).

Comparison of the neck's range of motion of both groups revealed that the right RNR of the NFL was significantly larger ($p = 0.026$). The right and left RNR were moderately correlated only in the NFL group, ($r = 0.698$; $p < 0.001$) (**Figure 2**), but there was no significant difference between left and right RNR of either group.

Table 2. Variance in the mean values (\pm standard deviation) of the 180° turn test, Timed Up & Go and 360° turn tests results by categories, in groups (Fallers and Non-Fallers, with and without a neck brace).

TEST	NFL ^a	FL ^a	p-value
180 TT			
Turn Time (sec)^b			
WOB	2.4 (\pm 0.5)	3.5 (\pm 1.1)	p < 0.001**
WB	2.6 (\pm 0.7)	3.9 (\pm 1.3)	p < 0.001**
p-value	p = 0.025*	p < 0.001**	
Number of steps			
WOB	3 (\pm 1)	4.5 (\pm 3.6)	p < 0.001**
WB	3.3 (\pm 1.1)	4.8 (\pm 1.4)	p < 0.001**
p-value	p = 0.074	p = 0.028*	
Total score (0 - 8 pts.)^c			
WOB	2.7 (\pm 1.5)	4.8 (\pm 1.4)	p < 0.001**
WB	3.4 (\pm 1.7)	5.2 (\pm 1)	p < 0.001**
p-value	p = 0.004**	p = 0.005**	
TUG			
WOB	10.7 (\pm 2.8)	18.5 (\pm 7.4)	p < 0.001**
WB	11.7 (\pm 3.7)	19.3 (\pm 7.3)	p < 0.001**
p-value	p = 0.004**	p = 0.172	
360 TT			
Turn Time (sec)			
WOB	4.4 (\pm 1.3)	7.4 (\pm 2.9)	p < 0.001**
WB	4.8 (\pm 1.8)	7.8 (\pm 2.9)	p < 0.001**
p-value	p = 0.004**	p = 0.057	
Number of steps			
WOB	7.5 (\pm 1.6)	10.3 (\pm 2.7)	p < 0.001**
WB	7.9 (\pm 1.9)	11.1 (\pm 3.1)	p < 0.001**
p-value	p = 0.022*	p = 0.004**	

Note: 180 TT, 180° Turn Test; TUG, Timed Up & Go Test; 360 TT, 360° Turn Test; WOB, Without a neck brace; WB, with a brace. ^aNFL-No reported falls during past year, FL-Fell twice or more during the past year. ^bTime to accomplish a turn. ^c180 TT parameters evaluated were gradation of staggering, number of steps, time to accomplish a turn and turn strategy. The score given was 0 - 2 for each section and was inversely proportional to the level of performance. *p < 0.05; **p < 0.01.

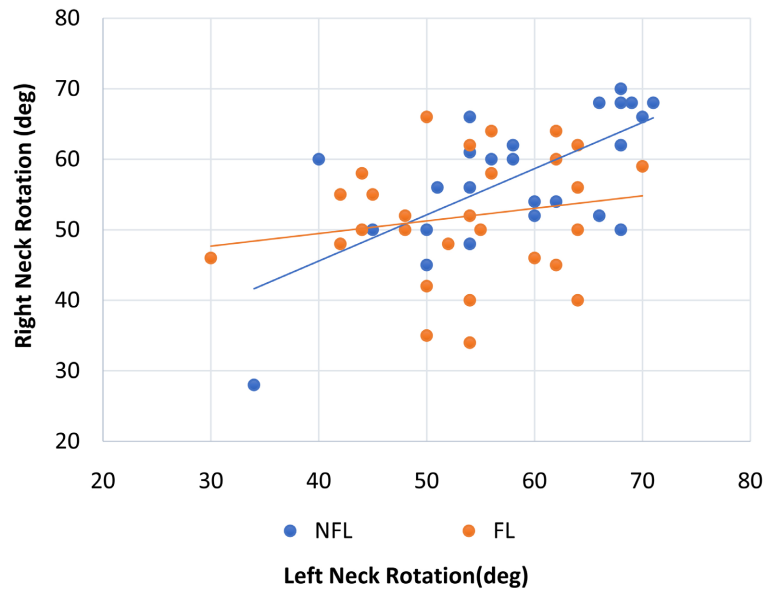


Figure 2. Scatterplots of right and left RNR of the FL and the NFL. The correlation between the right and the left RNR of the NFL and the FL was 0.698 ($p < 0.001$) and 0.181 ($p = 0.348$), respectively.

Table 3. Spearman correlations between cervical spine range of neck rotation with the age, number of falls, and balance measurements (Timed Up & Go, 180° Turn test, 360° Turn test) of all participants (N = 59).

Variable	Right cervical spine rotation		Left cervical spine Rotation	
	Correlation Coefficient	p-value	Correlation Coefficient	p-value
Age (years)	-0.269*	0.039	-0.196	0.136
Number of falls in past year	-0.272*	0.037	-0.151	0.253
Mean value of outcome measurements (Without a Brace)				
Timed Up & Go	-0.284*	0.029	-0.083	0.532
180° turn test score	-0.342**	0.008	-0.033	0.806
360° turn test (number of steps)	-0.370**	0.007	-0.016	0.909
360° turn test (time taken to accomplish turn)	-0.365**	0.008	-0.025	0.863

* $p < 0.05$; ** $p < 0.01$.

There was also a low but significant correlation between the right RNR, the number of falls ($r(s) = 0.272$; $p < 0.05$) and the equilibrium tests, with correlation strength ranging between $r(s) = 0.284$; $p < 0.05$ and $r(s) = 0.370$; $p < 0.01$) (Table 3). The correlation of the right RNR was slightly stronger with the values of the balance tests WOB than WB.

To predict the risk of falling, a logistic regression of the right neck rotation was conducted. Calculation of the odds ratio for 5° and 10° limitations in the right RNR revealed an increase of 1.41 and 1.99, respectively. Implying that those limitations increase the odds of falling by about one and a half and twice as much, respectively.

5. Discussion

The demographic data of the participants in present study is consistent with previous studies that dealt with different perspectives of turning and falls [11] [27]. More so, the scores of the various sections of the 180 TT and of the TUG obtained in the present study, matched those of Gamerman *et al.* [27]. For example, average NFL, TUG score of 10.7 ± 2.8 versus 10.49 ± 3.19 and for the FL 18.5 ± 7.4 versus 18.65 ± 8.29 , respectively. In addition, the correlation coefficient between the TUG and 180 TT scores was 0.888 ($p < 0.01$) in the present study and 0.881 ($p < 0.01$) in the study of Gamerman *et al.* The data of the 360 TT in the current study is also consistent with the values obtained by Dite and Temple ($r = 0.82$ and $r = 0.76$, respectively) [26]. On the other hand, the number of steps required for a 360° turn appear to differ slightly from the findings of Lipsitz *et al.*, who have reported that 66% of the FL, performed the turn with more than 12 steps compared to 10.3 steps in the current study [23]. This difference can be explained by older average age (87 years) and inclusion of various diseases, not included in the present study.

The restriction of neck mobility has significantly degraded the performance of most stability tests except the FL turning time of 360 TT, which approached statistical significance ($p < 0.057$) and the TUG score ($p < 0.172$) (Table 2). The divergence of the TUG test was probably due to the standing up and walking components of the test, which do not require turning and constitute about two thirds of the TUG duration. It is also conceivable that adults who have fallen in the past have modified their gait strategy and walk slowly and cautiously to begin with, regardless of the neck restriction [23].

There was a significant difference between the stability scores of both groups, but the scores of both groups were not affected differently by the neck restriction. The failure to reject the hypothesis of interaction may stem from a compensatory balance strategy of the fallers which might have embraced a different turning strategy, such as slowing down [23], increasing the steps' number [9] [28], and advancing the transverse pelvic rotation ahead of the trunk's rotation [17]. The higher steps' number of the FL during the 180 TT WOB (4.5 vs 3, $p < 0.01$ for the FL and NFL, respectively), lends support to such modification. The stepping strategy of the FL may also facilitate balance control and coordination by rotating the body more "en bloc", reducing the range of the transverse rotation between the pelvis and the thorax [17] [28]. Such stepping strategy may also require less RNR than the spin strategy, as evidenced by the resilient of the TUG performance of the FL, to neck bracing. The shift from a pivoting to stepping

strategy is also in line with the turning model of top down and bottom up, in which the head or base of support, respectively, serves as a frame of reference [29].

Although there was no interaction between bracing and group, the balance scores of both groups decreased by neck bracing and the scores of the FL with and without a brace were lower than the equivalent scores of the NFL. This finding has direct clinical ramifications since injured neck is often managed by a neck brace or other stabilization procedure [30]. Hence, following a neck bracing it is highly recommended to assess the balance of those adults and to consider safety precautions as using of a gait assistive device or modification of the environment.

An additional finding was that the FL participants had a significantly lower range of neck rotation to the right than the NFL. The lower RNR of the FL may be due to the higher age of the FL, but apparently, the age difference was minimal since the age of most participants in the FL ($N = 23$) and the NFL ($N = 21$) ranged between 70 - 89.9 with an average age of 79 versus 77, respectively.

Although there was no significant difference between the right and the left RNR within each group, there was a striking difference between the correlations of both sides. The Correlation of the right and left RNR of the NFL was 0.698 ($p < 0.001$) while that of the FL was only 0.181 ($p = 0.348$) (Figure 2). Apparently, although the decrease of the right RNR of the FL was not sufficient for affecting the bilateral similarity of the range of motion, it has still distorted the collinearity between the left and right RNR.

Interestingly, the right RNR of all participants was significantly correlated with age, number of falls, stability tests WOB and group affiliation. The level of those correlations was low to moderate, but still statistically significant and consistent. Removing the data of the eldest age group (90 years or older), did not markedly affect the correlations between right RNR and the stability tests, suggesting that age is not the major factor in this association. Since only the right rotation was correlated with the stability tests, the likelihood of falling was calculated only with reference to right RNR. The computation revealed that a decrease of around 10 degrees in right RNR may double the odds of falling. Therefore, limited right RNR should be considered a risk factor for falling.

A possible explanation for the lateralized association of the neck's rotation with stability parameters is provided by Wallwork *et al.* who suggest that the motor imagery of right head rotation is more vigorously represented in the motor and perceptual areas of the cerebral cortex [31], in line with the favored right head rotation of neonates [32]. Biasing toward right head rotation was also reported during the maneuver of kissing [33] and during generation of random numbers [34]. Moreover, examination of the neck muscles of older adults revealed characteristic unilateral weakness of the left neck muscles (which are the agonists for right head turning), and was suggested as a risk factor of traumatic brain injury (TBI) resulting from falls [35].

The behavioral laterality of the neck's rotation was attributed to cultural norms, neurophysiological asymmetry and to the lateralized abstract perception of the physical world [36]. To the best of our knowledge the present study is the first one to associate the lateralization of the neck rotation with balance impairment, of older adults. Further studies, associating the unilateral neck rotation with balance control, are warranted.

6. Limitations

About 38% of the FL were treated during the past year in a fall prevention group. Those practicing sessions might have skewed the results of the balance tests. However, as noted above, the stability scores matched the scores of previous studies.

Generalization of the findings is applicable to the studied age group (76 ± 6.9 years). The findings are not applicable to individuals with neurological disorder. Considering that most participants were women (49 Vs 10), the findings are probably more applicable to women.

There are also limitations concerning study blindness. The TUG score was measured and recorded by the main researcher who was aware of the group's affiliation. It is, however, an objective test, robust to external influence. Moreover, the data from the 180 TT and 360 TT tests were analyzed by two researchers, separately, ensuring that the films did not include information on the participant's group.

The recording of only the lateral view may have hindered the analysis of the turn characteristics. Shooting from additional angles would have made it easier to see the initiation of the 180° turn.

To overcome the difficulties that arose from the filming technique, the video clip analysis was performed by two researchers. First, each researcher analyzed the clip separately. Then, the findings were compared, any discrepancy was discussed, and a joint decision was made.

7. Conclusions

With or without a neck brace, most stability scores of adults with a fall history were lower than those of the non-fallers. Limiting of the neck rotation reduced turning stability of both groups, however there was no difference between the restriction effect on both groups. The findings of this study suggest that following any restriction the neck's mobility of older adults it is important to assess their stability and to consider using of a gait assistive device.

Interestingly, only the range of the right neck rotation was found to be correlated with number of falls and the scores of turning stability. The unilateral association of the RNR with the balance performance may portray a single domain of a general lateralization phenomenon of the motor and perceptual systems.

This study reinforces the need for evaluating the neck's range of motion during stability assessment and training of older adults. Routine guidance of older adults on maintaining appropriate neck mobility may assist to prevent falls with

all its adverse impacts.

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Informed Consent

All participants signed an informed consent.

Ethics Approval

The study was approved by the Ethics Committee of Clalit Health Services (0131-17-COM2). We certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Authors' Contribution

All authors contributed to the concept and design, recruitment of subjects or acquisition, analysis, and interpretation of data. All authors read and approved the final manuscript.

Availability of Data and Material

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent of Participants

Consent was provided in compliance with ethical standards and Declaration of Helsinki.

Conflicts of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest. The authors have no financial or proprietary interests in any material discussed in this article.

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