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1 **Changes in the ankle muscles co-activation pattern after 5 years following total ankle joint replacement**

2

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27

28 **ABSTRACT**

29 *Background:* The Hintegra[®] arthroplasty provides inversion-eversion stability, permits axial rotation, ankle
30 flexion-extension, and improvements of the gait patterns are expected up to 12 months of rehabilitation.
31 However, sensorimotor impairments are observed in ankle flexors/extensors muscles after rehabilitation, with
32 potential negative effects on locomotion. Here we determined the timing and amplitude of co-activation of the
33 tibialis anterior and medial gastrocnemius muscles during gait by assessing non-operated and operated legs of
34 patients with total ankle replacement, 5 years after surgery.

35 *Methods:* Twenty-nine patients (age: 58 [5.5] years, height: 156.4 [6.5] cm, body mass: 72.9 [6.5] kg, 10 men,
36 and 19 women) that underwent Hintegra[®] ankle arthroplasty were included. Inclusion criteria included 5 years
37 prosthesis survivorship. The onset and offset of muscle activation (timing), as well as the amplitude of
38 activation, were determined during barefoot walking at self-selected speed by surface electromyography. The
39 timing, percentage, and index of co-activation between the tibialis anterior and medial gastrocnemius were
40 quantified and compared between non-operated and operated legs.

41 *Findings:* The operated leg showed higher co-activation index and temporal overlapping between tibialis
42 anterior and medial gastrocnemius during gait ($P < .001$).

43 *Interpretation:* The neuromuscular changes developed during the process of degeneration do not appear to be
44 restored 5 years following arthroplasty. The insertion of an ankle implant may restore anatomy and alignment
45 but neuromuscular adaptations to degeneration are not corrected by 5 years following joint replacement.

46

47

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51 *Keywords:* EMG; joint stiffness; total ankle replacement; walking; gastrocnemius; tibialis anterior.

52 **1. Introduction**

53 Lower limb osteoarthritis is associated with pain and impaired function with negative effects on locomotion.
54 More specifically, ankle osteoarthritis impairs sagittal plane motion (dorsiflexion and plantarflexion) and torque
55 (Al-Mohrougi et al., 2018). In many cases the joint degeneration will reach levels that require the total joint
56 replacement. Ankle arthroplasty is a surgical procedure in which the tibiotalar joint is replaced (Giannini et al.,
57 2000; Caravaggi et al., 2015). Eighty percent of candidates are patients who developed ankle osteoarthritis
58 secondary to trauma (post-traumatic etiology) (Horisberger et al., 2009; Bloch et al., 2015), with far fewer
59 outcomes reported compared to hip and knee arthroplasty (Al-Mohrougi et al., 2018). In the past 40 years more
60 than 30 models of ankle prosthesis have been introduced, with few outcomes against hip and knee arthroplasty
61 (Giannini et al., 2000; Henricson et al., 2011). In this regard, Hintegra[®] arthroplasty is a third generation
62 prosthesis that provides inversion-eversion stability, permits axial rotation, ankle flexion-extension being one of
63 the few ankle prosthesis showing good results concerning activities of daily living (Michael et al., 2008;
64 Hintermann, 2005). Previous studies showed that the Hintegra prosthesis is built with stable components, with
65 low rate of complications (Michael et al., 2008; Hintermann, 2005; Barg et al., 2011), allowing an adequate
66 range of motion (Valderrabano et al., 2003; Michael et al., 2008; Hintermann, 2005). However, the lack of
67 restoration of gait symmetry and joint function remains a problem after ankle arthroplasty (Caravaggi et al.,
68 2015).

69 During the first year after Hintegra[®] arthroplasty, there are adaptations in the first three months of
70 rehabilitation that negatively affects the gait biomechanics. These include lower maximal plantar-flexion
71 moment, total adduction moment, medial ground reaction force, and higher anterior ground reaction force
72 during gait by increasing mechanical loading on knee joint (Valderrabano et al., 2007). This adaptive period was
73 previously reported as negative phase of rehabilitation (De la Fuente et al., 2014). These parameters are
74 expected to improve towards the end of the first year after surgery (Valderrabano et al., 2007), with significant
75 improvement of gait pattern (Valderrabano et al., 2007; Aidi et al., 2013) and quality of life (Esparragoza et al.,
76 2011). It has been suggested that 5 years following total ankle joint replacement there is an increase in the
77 American Orthopaedic Foot and Ankle Score (Zaidi et al., 2013). However, there is little information
78 concerning the effect of ankle replacement on neuromuscular activity of ankle muscles (tibialis anterior and
79 medial gastrocnemius) (Doets et al., 2007). Abnormal muscle co-activation could result in increased and
80 abnormal kinetics on the prosthesis predisposing to loosening. Presumably the prosthesis is designed to replicate

81 normal anatomy of the ankle joint. If however the muscular co-activation does not change the forces will remain
82 high.

83 An adequate control of tibialis anterior and medial gastrocnemius muscles depends both on the timing of
84 agonist and antagonist activation (Hubley-Kozey et al., 2010; Rosa et al., 2010), and the intensity of their
85 contractions, i.e. weight coefficients (Cappelini et al., 2006). These muscles sometimes present co-activation, an
86 involuntary and concurrent activation of the antagonist, in opposition to the contraction of the agonist
87 (Duchateau et al., 2014). Changes in co-activation occur during different physical activities e.g. running
88 compared to walking (Cappelini et al., 2006), footwear selection (Alkjær et al., 2012) and in pathological
89 processes e.g. cerebellar ataxia (Mari et al., 2014), foot and knee motor functions (Di Nardo et al., 2015), and
90 ankle osteoarthritis (Von Tscharnner & Valderrabano, 2010). Furthermore, co-activation may affect gait pattern
91 and the integrity of prostheses due to abnormal joint force development (De la Fuente et al., 2014).

92 After the Hintegra[®] arthroplasty placement, the gait pattern is expected to be restored, and co-activation
93 between tibialis anterior and medial gastrocnemius should not occur at medium term after the first three months
94 of rehabilitation (Michael et al., 2008; Hintermann, 2005). However, there is a lack of evidence concerning
95 patterns of co-activation after ankle replacement when rehabilitation is completed. Therefore, here we determine
96 the relative measures of amplitude and timing of co-activation of the tibialis anterior and medial gastrocnemius
97 muscles during gait, by comparing the electromyographic activity of the non-operated and operated leg of
98 patients with total ankle replacement, 5 years after surgery. Our null-hypotheses were: i) total ankle replacement
99 after 5 years does not recover the timing of co-activation to the level of the non-operated leg during gait; ii) total
100 ankle replacement after 5 years does not recover the temporal percentage of co-activation to the level of the non-
101 operated leg during gait, and ii) total ankle replacement after 5 years does not recover the index of co-activation
102 to the level of the non-operated leg during gait.

103

104 **2. Methods**

105 2.1. Study design

106 This is a cross-sectional, observational, analytical study design. The sample included twenty-nine patients (10
107 men and 19 women) that underwent unilateral total ankle replacement 5 years before the measurement session
108 in which the operated and non-operated leg were compared during gait. The inclusion criteria were: i) unilateral

109 total ankle replacement with Hintegra[®] arthroplasty (Newdeal SA, Vienne, France); ii) at least 5 years following
110 replacement; iii) rehabilitation treatment of one year; iv) posttraumatic arthritis; v) age between 40 and 70 years
111 old; vi) passive dorsal range of motion greater than 5° at the sagittal plane (De la Fuente et al., 2014); vi)
112 radiological stability (Horisberger et al., 2009; Bai et al., 2010; Guyer and Richardson, 2008); and v) have been
113 rehabilitated at the *Instituto Traumatológico* (Santiago, Chile) by the same surgical and rehabilitation team. The
114 exclusion criteria were: i) need for assisted locomotion; ii) major limitations in performance of daily life
115 activities; iii) major periarticular tissue impairment; iv) ipsilateral or contralateral hip/knee osteoarthritis; v)
116 inflammatory diseases; vi) neurological pathology; vii) active infection; and viii) cognitive impairment (von
117 Tschärner and Valderrabano, 2010). This study was approved by the institutional review board of the *Instituto*
118 *Traumatológico* (Santiago, Chile) according to the principles of the Declaration of Helsinki. All participants
119 signed a consent term agreeing to participate in this study.

120

121 2.2. Sample size

122 The sample size was estimated “a priori” with a pilot experiment that included 6 patients [mean (standard
123 deviation) 56.5 (2.1) years-old, 30.1 (1.8) kg/m², 3 men and 3 women] that fulfilled the inclusion and exclusion
124 criteria. A sample size of 23 patients was estimated considering a difference between two dependent means
125 (matched pairs), using two-tailed *t*-test with alpha error of 5% and statistical power of 80% for an estimated
126 effect size of 0.62. Six additional patients were included to the sample to anticipate possible attrition (20% of
127 estimation). The total patients assessed were 35 patients; 6 patients from the “a priori” determination of sample
128 size and additional 29 patients. The statistical calculus was performed by G*Power software version 3.1.9.2.
129 (Kiel University, Germany).

130

131 2.3. Surgery and physical therapy procedures

132 All participants had a Hintegra[®] prosthesis (Hintermann, 2005) (Newdeal SA, Vienne, France). In general terms,
133 surgery involved an anterior longitudinal incision of 10 to 12 cm performed to dissect the retinaculum.
134 Moreover, the soft tissue and periosteum from the bone were dissected. Resection of the talus and tibia were
135 performed to insert arthroplasty components using Hintermann[®] distractor and oscillating saw. Osteophytes on
136 the talar neck and anterior aspect of medial malleolus were also removed. After that, the tibial and talar

137 components were inserted. The last inserted component was the polyethylene component. The tissues were
138 sutured, and the procedure was finalized by fitting a short leg cast. The patients were monitored for the next
139 three weeks after surgery, once per week, and during the first 4 weeks after surgery patients were immobilized
140 with a short leg cast and instructed to unload the operated leg and rest.

141 The physiotherapy intervention was performed from week 4 until week 52 (Ingrosso et al., 2009).
142 From the week 4 to 12, the patients attended the rehabilitation service, where they used a walking boot. In this
143 period, partial weight bearing was permitted using the assistance of canes. Furthermore, stretching to improve
144 the dorsal flexion range of motion, strengthening of ankle, knee and hip muscles, and pain relief with physical
145 agents were activities performed. The re-education of gait without assistance, bipedal heel rise, balance
146 exercises, and pain relief management were performed until the end of week 52 (Martin et al., 2007).
147 Afterwards, patients returned to the to the foot and ankle hospital unit every six months to be assessed in the
148 follow-up period.

149

150 2.4. Data acquisition and processing

151 The data acquisition consisted of two stages: clinical assessment and surface electromyography recordings. The
152 patients attended an interview, and the clinical assessment was performed at the foot and ankle service of the
153 *Instituto Traumatológico* (Santiago, Chile). The age, body mass, height, AOFAS score (Kitaoka et al., 1994),
154 passive dorsiflexion range of movement, difference in calf whilst standing (Saxena et al., 2011; Valdebarrano et
155 al., 2006), and intensity of pain at rest and during walking assessed with a numerical verbal scale (0 no pain, 10
156 maximum possible pain) (Hintermann, 2005) and were part of the clinical assessment.

157 Surface electromyography recordings were performed one week after the clinical assessment at the
158 *Centro de Investigaciones Medicas del Instituto Traumatológico* (Santiago, Chile). After a 5-min warm-up on a
159 cycloergometer without external load and cadence of 60 rpm, patients walked barefoot at self-selected speed
160 (von Tscharnier and Valdebarrano, 2010; De la Fuente et al., 2014) along a 5-meter flat surface on a straight-
161 line. Patients performed five trials for familiarization within the walking space. Although we did not measure
162 kinematics, a common heel strike pattern was observed among the patients. The electromyography signals were
163 acquired during walking using a Myomonitor IV electromyography amplifier (Delsys, inc., Boston, USA). Two
164 DE-2.3 single differential surface electromyography sensors (Delsys, inc., Boston, USA) with an inter-electrode

165 distance of 10 mm were used. The data collection employed a 16-bit analog-digital converter card (National
166 Instrument Corp., Austin, TX, USA) operated by a Matlab software (Mathworks Inc., Massachusetts, USA) at a
167 sampling rate of 1000 Hz, band-pass filtered (20–450 Hz), and hardware amplified with a gain of 1000 V/V.
168 The muscles assessed were tibialis anterior and medial gastrocnemius based on their lower mean
169 electromyography frequency and intensity previously found by Valderrabano et al. (2006) in unilateral ankle
170 osteoarthritis, and the hypothesis of Doets et al. (2007), who suggested that after ankle joint replacement, higher
171 co-activation between these muscles could exist during gait. The surface electromyography sensors were placed
172 according to the European recommendations for surface electromyography (Hermens et al., 2000).

173

174 2.5. Signal treatment

175 The electromyography signals were filtered by a zero-lag 4th order finite impulse response Butterworth with a
176 band pass of 20 to 450 Hz. Onset and offset times of muscle activation (Caravaggi et al., 2015) were identified
177 using a continuous wavelet with the algorithm proposed by Merlo et al. (2003). The algorithm was performed
178 using the Hermite-Rodriguez mother wavelet, 10% of noise power, 150 ms for the time of two detected
179 activation intervals, and 5 ms for the spike rejection from non-rectified signals. The noise of electromyography
180 signals was extracted when patients stood quietly before walking. Five consecutive electromyography bursts of
181 the tibialis anterior and gastrocnemius medialis (corresponding to 5 strides) were used for the analysis.

182 All signals were full wave rectified (Figure 1). Due to the variability and non-accordance of
183 normalization methods for analysis of electromyography signals (Rosa et al., 2010), a standardized treatment of
184 signals by z-score method was performed. Each sample was subtracted from its expected value ($E[X]$) and
185 divided by the standard deviation. This expresses the number of standard deviations by which the sample is
186 above the $E[X]$. As the whole electromyography signals showed a normal distribution, the z-score was obtained
187 using the arithmetic mean of the data.

188

189 2.6. Outcomes

190 *The timing of co-activation:* determined by the time overlap between the onsets and offsets activation (Rosa et
191 al., 2010).

192 *Percentage of co-activation*: from the time activation onsets and offsets, the percentage of co-activation was
193 quantified as the overlapped percentage of muscle activation (Rosa et al., 2010).

194 *Co-activation index*: determined by the overlapped amplitudes of muscle activation between the tibialis anterior
195 and medial gastrocnemius. The co-activation index was implemented in discrete form by the trapezoidal method
196 (Eq. 1) from the original continuous form previously defined in the literature (Rosa et al., 2010).

197

$$198 \quad Coactivation\ index = 2 \times \frac{\sum_{CoAc_{onset}}^{CoAc_{offset}} \left[\frac{(X_{i+1} - X_i)}{2} \times \Delta t \right]}{\sum_{Agonist}^{Antagonist} \left[\sum_{onset}^{offset} \frac{(X_{i+1} - X_i)}{2} \times \Delta t \right]_j} \times 100\% \quad (Eq. 1)$$

199

200 In the equation 1, $CoAc_{onset/offset}$ is the co-activation time of onset or offset, x_i is the electromyography
201 sample, Δt is the interval time of data acquisition given the sampling frequency, and j represents the agonist or
202 antagonist condition. To assess the intensity of concurrent contractions, the trapezoidal areas were obtained
203 using the “cumtrapz function” from the full-rectified signals using the Matlab software (Mathworks Inc.,
204 Massachusetts, USA).

205

206 2.7. Statistical analysis

207 Data were reported as the median and interquartile range [IQ range] because the Shapiro-Wilk test revealed a
208 non-parametric data distribution. Homoscedasticity was confirmed using the Levene’s test. To compare the
209 timing, percentage, and index of co-activation of medial gastrocnemius and tibialis anterior between the
210 operated and non-operated legs, a Wilcoxon Signed-Ranks test of two-tails was used with alpha error equal to
211 5%. To assess the possible existence of co-variable and interaction with outcomes, a multiple regression respect
212 to analysis for age, body mass, height, AOFAS score, the passive dorsal range of movement, calf circumference
213 difference between leg during a standing posture, the intensity of pain at rest and during gait were considered at
214 $p < 0.05$. Data were analyzed using the Matlab software statistical toolbox (Mathworks Inc., Massachusetts,
215 USA).

216

217 **3. Results**

218 The timing of co-activation between the tibialis anterior and medial gastrocnemius in the non-operated leg
219 [median: 390 ms, IQ range: 80 ms] was lower than in the operated leg [median: 566 ms, IQ range: 104 ms,
220 $p<0.001$]. The percentage of co-activation between the tibialis anterioris and gastrocnemius medialis in the non-
221 operated leg [median: 0.00 %, IQ range: 1.84 %] was lower than in the operated leg [median: 100%, IQ range:
222 0.00 % $p<0.001$]. The index of co-activation between the tibialis anterior and medial gastrocnemius in the non-
223 operated leg [median: 0.00 %IQ range: 1.94 %] was lower than in the operated leg [median: 30.96%, IQ range:
224 13.52%, $p<0.001$]. The changes in co-activation are depicted in the Figure 1.

225 The demographic characteristics of the sample regarding age, body mass, height, AOFAS score,
226 passive dorsal range of movement, calf circumference difference between legs during standing posture, intensity
227 of pain at rest, and during gait did not co-vary or interacted with any of the electromyography outcomes
228 ($p>0.05$).

229

230 *** Table 1 around here ***

231 *** Figure 1 around here ***

232

233 **4. Discussion**

234 The most important finding of this work was that patients with the Hintegra® arthroplasty present abnormal
235 plantar and dorsi-flexion co-activation patterns during gait after 5 years following total ankle joint replacement.
236 Although the patients did not receive rehabilitation after 5 years following total ankle joint replacement due to
237 the improvement observed in the AOFAS score, the present findings suggest the need for an appropriate
238 sensorimotor rehabilitation program for patients in which problems at medium term of survival of the prosthesis
239 still persist.

240 Although it can't be ensured (due to the lack of kinetics and kinematics assessment), the altered co-
241 activation found in our study may suggest that both absorption and propulsion phases of walking could be
242 committed 5 years after replacement surgery. Dorsal and plantar-flexor muscles need to be activated during
243 different phases of gait in order to maintain the normal mechanics of the ankle joint during swing and load

244 response. This is important for the control of the anterior advance of the tibia or the generation of propulsion.
245 Therefore, these mechanical actions need temporal muscle coordination (timing of activation). Based on the
246 findings from Di Nardo et al. (2015) and Cappellini et al. (2006), the tibialis anterior and medial gastrocnemius
247 muscles should present independent temporal activations during the different phases of normal gait (low speed).
248 It contrasts with the results of patients treated with ankle prosthesis, since a temporal overlap between these
249 muscles was found.

250 Based on the findings from Siegler et al. (2013), an altered kinetic condition can be present in patients
251 with Hintegra[®] arthroplasty. Siegler et al. (2013) tri-dimensionally modeled the talus of 26 healthy adults and
252 found that “the trochlear surface can be modeled as a skewed truncated conic saddle shape with its apex oriented
253 laterally rather than medially”, which contrasts with the mechanical model of Inman, in which the Hintegra[®]
254 arthroplasty is based (Hinterman 2005). Thus, the mechanical design of the Hintegra[®] arthroplasty could alter
255 distribution or intensity of ankle joint forces during the stance phase, or both, such as the abnormal joint shear
256 forces and delayed the first peak of vertical ground reaction force found after the negative rehabilitation phase in
257 patients treated with an Hintegra[®] arthroplasty (De la Fuente et al., 2014). Our data suggests that these
258 mechanical changes could result of sensorimotor adaptations, since an increased co-activation between dorsal
259 and plantar flexors would reduce the velocity of the foot and tibia during stance phase, which reduces the
260 vertical component of the ground reaction force at load response phase. However, an increased co-activation
261 might also result of intrinsic instability of the prosthesis in the frontal plane, which could have an unstable effect
262 over the foot based on mechanical findings from Siegler et al. (2013), further leading to the shifting of the
263 medial gastrocnemius rather than a shift of the tibialis anterior activation, as shown here.

264 As the shifting in the medial gastrocnemius could occur, the propulsion phase might also be affected
265 (Giannini et al., 2000; Henricson et al., 2011). This possible change is in accordance with de la Fuente et al.
266 (2014), who proposed a gait pattern with external hip rotation that increases the activity of hip extensors (rather
267 than plantar flexors) to generate the propulsion of the leg with Hintegra[®] arthroplasty, after the negative
268 rehabilitation phase. Therefore, it is possible that patients with Hintegra[®] arthroplasty experience an over-
269 stabilization of the ankle joint after at medium term, affecting the whole pattern of gait by an unstable load
270 response and altered propulsion phase. This hypothesis still needs to be investigated.

271 On the other hand, Stubbs et al. (1998) suggested that the load over viscoelastic tissues creates a
272 sensorimotor response called “muscle-ligament reflex” causing an altered activity of agonist and antagonist

273 muscles over time. Therefore, the surgery itself could cause the neuromuscular changes observed, since the
274 tibialis anterior and ankle ligaments must be pulled to introduce the arthroplasty components into the ankle joint
275 space. This is important as one wonders if neuromuscular changes are reversible with time. Our findings would
276 suggest that at 5 years after ankle replacement they are not reversible. In making this statement perhaps
277 prosthesis designers would be better to use an arthroplasty designed to tolerate the irreversible forces on the
278 prosthesis. Finally, chronic pain could be another source of the neuromuscular changes observed in our study.
279 Valderrabano et al., (2006) and von Tscharnner et al. (2010) described that the time of exposure to pain in
280 osteoarthritis is the worst stimulus to the nervous system changing the neuromuscular patterns of activations.
281 This could induce changes in the ankle stiffness leading to pathological neuroplasticity changes, possibly
282 present since before the arthroplasty surgery. However, in our study, the intensity of pain was not identified as a
283 co-variable and did not show any interaction with the outcomes.

284 Due to the higher co-activation found in patients with Hintegra[®] arthroplasty at 5 years after ankle
285 replacement, new rehabilitation approaches are needed to improve the locomotion in patient who shows the
286 sensorimotor impairments described here. To our knowledge, this is the first pathological report at medium term
287 in patients with Hintegra[®] arthroplasty. Future studies should identify *in vivo* whether the ankle axis of this
288 arthroplasty is really positioned as Inman previously reported, since alterations in the prosthesis axis of rotation
289 could lead to the sensorimotor impairments found. Also, the presence of other concomitant musculoskeletal
290 problems (e.g., knee, hip or trunk disorders, metatarsal-cunieform, cunieform-navicular and talo-navicular
291 osteoarthritis) requires further examination. Finally, it is important to investigate whether previous pathological
292 sensorimotor conditions acquired before the arthroplasty are irreversible after the surgery (i.e., chronic pain).
293 Regarding the limitations of our study, the sample is only representative of patients with lower AOFAS score, in
294 contrast to the results with Hintegra[®] (Hinterman, 2005) and other arthroplasties (Aidi et al., 2013; Caravaggi et
295 al., 2015). Also, the measurement of pain considered a verbal pain scale (Hinterman, 2005), which may not
296 reflect the sensorimotor impartments showed by previous studies (Ervilha et al., 2004; Lindstrøm et al., 2011).
297 Finally, we propose that a detailed mechanical analysis of gait, in addition to the analysis of co-activation
298 alteration, is needed to understand the possible neuro-mechanical pathological new hypotheses discussed in our
299 study.

300

301 **5. Conclusions**

302 Altered co-activation during gait is present after at 5 years after total ankle replacement with the Hintegra®
303 prosthesis. It may result of an attempt to compensate ankle instabilities following arthroplasty, which effects on
304 gait dynamics require attention during rehabilitation programs.

305

306 **Conflict of interests**

307 The authors declare no conflicts of interest.

308

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396

397 **Figure caption**

398 **Figure 1. Temporal co-activation between medial gastrocnemius and tibialis anterior during gait in the**
399 **non-operated (top) and operated (bottom) legs from patient 1.** The EMG signals of the medial
400 gastrocnemius are shown in light gray and positive values. The tibialis anterior signals are shown in dark gray
401 and negative values. The line shows the identified time of muscle activity as proposed by Merlo et al (2003).
402 The upper box shows the color intensity scale of the temporal overlapping relative to the medial gastrocnemius.
403 The bottom boxes show the intensity of each overlap found. The signals were normalized in function of z-score.