

UNIVERSIDAD DE MURCIA FACULTAD DE BIOLOGÍA

The role of iliopsoas muscle in the development of degenerative disease of the hip (Arthrosis)

El papel del músculo psoas-ilíaco en el desarrollo de la coxartrosis

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THESIS

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Realizada por Doña Yulia Suvorova Suvorova Dirigida por Don Aurelio Luna Maldonado Don José Emilio Muñoz Barrio

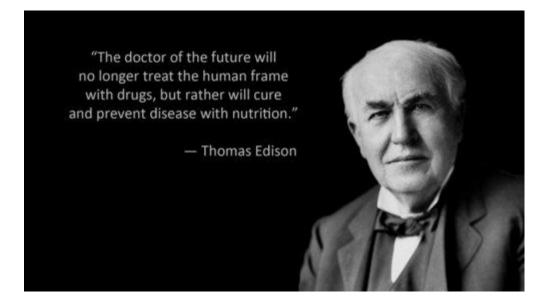
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"and the knowledge of the iliopsoas muscle"

--- Dr. R.E. Conger

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1 RESUMEN

IDEA GENERAL:

El músculo psoas-ilíaco (Iliopsoas) ha sido propuesto en los últimos tiempos por algunos autores como un factor de influencia en el desarrollo de Artrosis de cadera. Este proceso es lento y complejo, haciendo difícil su detección en el análisis estadístico.

ANTECEDENTES:

Un estudio anatómico publicado recientemente en la revista "American Journal of Sports Medicine" por Alpert, J.M., et al., (2010), identificaba por primera vez en la historia la anatomía de sección cruzada del conjunto de músculos conocido como psoas-ilíaco al nivel del labrum acetabular.

Un músculo psoas-ilíaco tirante o acortado puede ser causa de un aumento en la presión intra-articular así como de un síndrome de degeneración de la cadera, cursando con dolor, aparejado a él. A esta circunstancia hay que añadirle una posible irritación de la bolsa sinovial, chasquidos de cadera y un desplazamiento fallido de la pierna que en sí mismo puede causar una reacción en cadena de posteriores problemas en rodillas y pies. El aumento en la presión intraarticular puede desembocar en una cascada de efectos negativos en la articulación de la cadera resultando finalmente en pérdida de cartílago en la articulación y este hecho puede dar lugar a dolor, pérdida de movimiento, etc.

Una revisión de la literatura sobre el tema de la influencia de los músculos locales sobre la estabilidad de la cadera realizada por un equipo de investigadores australianos (Retchford, T.H., Crossley, K.M., Grimaldi, A., Kemp, J.L., Cowan, S.M., 2013) sugiere que los músculos locales de la cadera (Cuadrado Femoral, Glúteo Menor, Gemelos, Obturador interno y

externo, Iliocapsularis y las fibras profundas del músculo Psoas-Ilíaco), pueden ser considerados como estabilizadores primarios de la articulación de la cadera.

Antes de comenzar cualquier tipo de rehabilitación muscular global de pacientes con inestabilidad pasiva de la cadera puede ser conveniente realizar alguna intervención orientada a la restauración de alguna función neuromuscular aislada de los estabilizadores primarios de la cadera. Existe evidencia de que déficits en el labrum acetabular y en los ligamentos iliofemorales pueden conducir a una mayor traslación de la cabeza femoral y posiblemente a una patología degenerativa de la cadera. Pero, a pesar, de este papel "supuestamente" relevante se sabe poco sobre qué músculo o sinergia de músculos están implicados.

La degeneración de la cadera se consideró históricamente como idiopática por naturaleza y nunca como un proceso de enfermedad que pudiese ser alterado o detenido. A lo largo de esta tesis hemos pretendido desarrollar el conocimiento de este proceso con casos de estudio que muestren la posibilidad de detenerlo. La pérdida de movilidad asociada con los síndromes iliopsoáticos y la subsiguiente degeneración de la cadera no afectan tan sólo a la cadera y la pierna, pueden tener además un efecto negativo general sobre el estado de salud del paciente. A medida que el paciente reduce su actividad hay una reducción aparejada en su estado de forma general, reducción de su función metabólica (pudiendo dar lugar a un futuro síndrome metabólico), reducción de la actividad neurotransmisora del cerebro (con riesgo de depresión), reducción del rendimiento laboral, pérdida de empleo, distanciamiento con la sociedad, etc. Muchas de estas enfermedades y procesos sociales pueden ser evitadas con la simple detección de un acortamiento patológico en el músculo psoas-ilíaco.

Los costes resultantes sobre la sociedad se han disparado en los últimos años con la posibilidad de que la demanda de servicios por este motivo supere en un futuro cercano a la disponibilidad de cirujanos ortopédicos que puedan realizar estos procedimientos en la envejecida y sedentaria generación del "baby boom" de los países desarrollados.

El nivel de conocimiento disponible en el año 2014 sobre este tema no está al nivel que debiera debido a que los guardianes de esta información son también aquéllos que se benefician de no promover más investigación preventiva.

Un nuevo modelo se hace necesario en estos momentos para detener la degeneración de la cadera antes de que se alcance un punto en que la cadera necesite ser reemplazada.

DETALLES ANATOMICOS:

Si el músculo psoas-ilíaco está acortándose puede descompensar todo el sistema anatómico con las consecuencias de crear personas cargadas de espaldas, con postura desgarbada, o jorobadas. El músculo psoas-ilíaco acortado tirará del fémur produciéndose un efecto de torsión, un giro hacia fuera, y esta torsión puede también impedir que el pie descanse en horizontal sobre el suelo. El consiguiente giro del pie durante la marcha crea una fuente adicional de dolor y tensión. El psoas-ilíaco es sólo un músculo pero influye sobre toda una red de otros músculos. Los músculos del psoas-ilíaco son interdependientes, como los remeros de una carrera de embarcaciones. El término psoas-ilíaco hace referencia a la combinación del músculo psoas mayor y el músculo ilíaco en su extremo inferior. Estos músculos son distinguibles en el abdomen, pero, normalmente, no lo son en el muslo. Por este motivo reciben la denominación común de "iliopsoas".

La idea de la interacción entre el músculo psoas-ilíaco y la articulación de la cadera como causa de enfermedades de la cadera no es nueva ya que hay varias investigaciones que están enfocadas en esta dirección. Sin embargo, no hay evidencia científica que pueda probar esta intuición todavía.

OBJETIVOS:

El alcance de esta tesis es proporcionar alguna evidencia científica que contribuya al desarrollo del diagnóstico y la mejora en el tratamiento de la enfermedad degenerativa de la cadera.

El principal objetivo de la presente tesis doctoral es determinar la influencia de la debilidad del músculo psoas-ilíaco sobre la artrosis de cadera o coxartrosis.

Los objetivos secundarios son:

- Averiguar los factores que determinan la artrosis de cadera
- Crear perfiles de individuos que sean proclives a desarrollar artrosis de cadera en el futuro dadas sus características de hoy en día

HIPOTESIS:

La hipótesis de investigación a ser contrastada es que las características demográficas de los pacientes con el músculo psoas-ilíaco contraído pueden influir sobre el grado de gravedad de su artrosis de cadera.

ANALISIS ESTADISTICO:

Un estudio fue realizado en el centro del Músculo y las Articulaciones de Eindhoven (Países Bajos) durante el período comprendido entre Septiembre de 2011 y Septiembre de 2014. La muestra estaba compuesta por 400 pacientes de edades comprendidas entre los 30 años y los 80 años. De ellos la mitad eran hombres y la otra mitad mujeres. De acuerdo a la distribución de pacientes por edad éstos estaban equidistribuidos en los tres primeros tramos de edad (30-40, 41-50, 51-60), con una frecuencia igual a 100 casos para cada intervalo, y también estaban igualmente repartidos entre los dos últimos tramos de edad (61-70 y 71-80) con una frecuencia de 51 y 49 casos respectivamente. Respecto al tipo de artrosis la distribución de pacientes estaba claramente desnivelada a favor de la artrosis tipo II. Todos los pacientes presentaban dolor de cadera y varios niveles de degeneración de la cadera a la vista de los resultados obtenidos mediante radiografías o resonancias magnéticas. En el examen clínico todos los pacientes tenían acortado el músculo psoas ilíaco por 4-5 cm. El tratamiento consistió en manipulación lumbar, sacro ilíaca y de cadera seguida de alargamiento pasivo del músculo psoas-ilíaco realizado por un médico. El número de tratamientos recibidos por cada individuo de la muestra fue de siete.

Se realizó un análisis estadístico sobre la variable "**grado de gravedad de la artrosis de cadera**" a través de diferentes técnicas y métodos estadísticos. Esta variable se ha generado artificialmente a través de la combinación de otras dos variables que sí venían recogidas en la base de datos: "**Funcionalidad**" y "**Nivel de No-Dolor**". Ambas variables dieron lugar a una variable similar a la obtenida para la escala ASIA utilizada para medir el grado de gravedad de Lesión Medular. En la presente investigación hemos aplicado una escala similar pero con 3 grados de gravedad en lugar de 5, correspondiendo el grado "A" a más dolor y menos funcionalidad y el grado "C" a menos dolor y más funcionalidad, de acuerdo a la siguiente tabla:

NIVEL DE NO DOLOR	FUNCIONALIDAD RESIDUAL	GRADO DE GRAVEDAD
100%-89%	Total	A
88%-71%	En su mayoría	В

70 %-0%	Alguna	С

Con estos datos se aplicaron diversas técnicas de análisis multivariante:

Análisis Factorial Discriminante:

Esta técnica es una técnica de "clasificación" que consiste en la reducción de la escala del problema, aunque se puede aplicar igualmente aunque tengamos pocas variables en nuestra base de datos. Lo que hace la técnica es agregar las variables iniciales en un número menor de variables pero que contienen más información relevante sobre el comportamiento de la variable dependiente. Finalmente podemos establecer límites para cada región de la variable dependiente, es decir, las regiones "A", "B" y "C" y representar la función de correlación canónica en un par de ejes cartesianos y las regiones de "grado de gravedad de la artrosis de cadera" deberían estar separadas las unas de las otras y no superpuestas. También obtenemos una matriz de clasificación de cada paciente entre las categorías "A", "B" y "C".

Análisis de la Varianza (ANOVA):

Esta técnica no es una técnica de clasificación sino más bien una técnica de "Análisis Factorial" que determina si un factor como el género, la edad o el tipo de artrosis, influye sobre la variable dependiente en un determinado grado que ha de ser fijado por el investigador a través del "**Nivel de Significación**".

Necesita el cumplimiento de las hipótesis de Linealidad, Independencia, Normalidad y Homocedasticidad de los residuos del modelo.

Regresión Logística:

Esta técnica es una técnica de "Clasificación" que consiste en una clase específica de Modelo de Regresión Multivariable en la cual la variable dependiente es categórica, como en nuestra investigación. Esta técnica requiere el cumplimiento de las hipótesis generales del modelo (Linealidad, Independencia, Normalidad, Ausencia de Multicolinealidad, Ausencia de Autocorrelación) pero no requiere del cumplimiento de la hipótesis de "Homocedasticidad" de los residuos del modelo. Al final se obtiene una matriz de clasificación como la del Análisis Factorial Discriminante.

Análisis de Conglomerados:

Esta técnica no es de clasificación, sino más bien una técnica descriptiva. Su utilidad en nuestra investigación radica en que permite crear perfiles de pacientes de acuerdo a su grado de gravedad de artrosis muscular a partir de la información muestral, obteniendo de este modo un retrato robot de la clase de pacientes asignados a cada grado de gravedad de la artrosis de cadera.

El uso de diferentes técnicas de análisis multivariante, como las propuestas en la presente tesis, permite contrastar los resultados y minimizar la posibilidad de error, permitiendo un mayor enriquecimiento de los resultados, los cuales resumimos en la siguiente tabla:

			HIPOTESIS			RESULTAD		
						OS		
METOD	FACTOR	TECNICA	TIPO	TEST	SATIS	TEST	P-	SIGNIFIC
0					FECH		VAL	ATIVIDA
					Α?		OR	D
ANOVA	Género	T-Test	Normalidad	Muestra	S			
				Grande				

Tipo de	T-Test	Homocedas ticidad Normalidad	Levene	S	T-Test con aproximación de Welch	0,085	N
Tipo de Artrosis	1-Test	Normalidad	Grande	5			
		Homocedas ticidad	Levene	N	T-Test con aproximación de Welch	0,000	S
Edad	ANOVA Multifactor ial	Normalidad	K-S	N			
		Homocedas ticidad	Levene	N	F-Test	0,000	S
	Kruskal- Wallis	Homocedas ticidad	Levene	N	Chi-cuadrado Test	0,000	S
Interacción Género- Edad	ANOVA Multifactor ial	Normalidad	K-S	N			
		Homocedas ticidad	Levene	N	F-Test	0,447	N
Interacción Género- Tipo de Artrosis	ANOVA Multifactor ial	Normalidad	K-S	N			
		Homocedas ticidad	Levene	N	F-Test	0,993	N
Interacción Edad-Tipo	ANOVA Multifactor	Normalidad	K-S	N			

1		ial	[I
	de Artrosis	ial						
			Homocedas	Levene	N	F-Test	0,001	S
			ticidad					
	Interacción	ANOVA	Normalidad	K-S	N			
	Género-	Multifactor						
	Edad-Tipo	ial						
	de Artrosis							
				1			0.000	N
			Homocedas	Levene	N	F-Test	0,688	Ν
			ticidad					
ANALIS	Género	2 pasos	-	-	-			Alto
IS DE								impacto
CONGL								pero
OMERA								inconsist
DOS								ente
								•••••
	Tipo de	2 pasos	-	-	-			Irrelevant
	Artrosis							е
	Edad	2 pasos	-	-	-			Irrelevant
	Luau	2 pasus	-	-	-			
								е
ANALIS	Género	Correlacio	Normalidad	K-S	N	Lambda de	0,001	Bajo
IS		nes				Wilks		Impacto
FACTO		Canónica						pero
RIAL		S						inconsist
DISCRI								ente
MINAN								
TE								
			Homocedas	M de	N			
			ticidad	Box				

	Tipo Artrosis	de	Correlacio nes Canónica s	Normalidad Homocedas ticidad	K-S M Box	de	N	Lambda Wilks	de	0,001	Impacto medio pero inconsist ente
	Edad		Correlacio nes Canónica s	Normalidad	K-S		Ν	Lambda Wilks	de	0,001	Impacto medio pero inconsist ente
				Homocedas ticidad	M Box	de	Ν				
REGRE SION LOGIST ICA	Género		Máxima Verosimilit ud a través del Algoritmo de Newton- Raphson	Normalidad	K-S		N	Verosimilitu es	de ıd	0,689	N
	Tipo Artrosis	de	Máxima Verosimilit ud a través del Algoritmo de Newton- Raphson	Normalidad	K-S		Ν	Logaritmo Razón Verosimilitu es	de	0,000	S

Edad	Máxima	Normalidad	K-S	Ν	Logaritmo de	0,000	S
	Verosimilit				Razón de		
	ud a				Verosimilitud		
	través del				es		
	Algoritmo						
	de						
	Newton-						
	Raphson						
latere el Ce	Másima	N a waa a Kala al	Deserver	0		0.004	0
Interacción	Máxima	Normalidad	Pearson	S	Logaritmo de	0,001	S
Género-	Verosimilit				Razón de		
Edad	ud a				Verosimilitud		
	través del				es		
	Algoritmo						
	de						
	Newton-						
	Raphson						
Interacción	Máxima	Normalidad	Pearson	S	Logaritmo de	0,000	S
Género-	Verosimilit				Razón de		
Tipo de	ud a				Verosimilitud		
Artrosis	través del				es		
	Algoritmo						
	de						
	Newton-						
	Raphson						
Interacción	Máxima	Normalidad	Pearson	S	Logaritmo de	0,086	Ν
Edad-Tipo	Verosimilit				Razón de		
de Artrosis	ud a				Verosimilitud		
	través del				es		
	Algoritmo						
	de						
	Newton-						

	Raphson						
Interacción Género- Edad-Tipo de Artrosis	Máxima Verosimilit ud a través del Algoritmo de Newton- Raphson	Normalidad	Pearson	S	Logaritmo de Razón de Verosimilitud es	0,000	S

Los resultados obtenidos presentan inconsistencias dando lugar a cifras diferentes dependiendo de la técnica empleada. Pero hay también algunas similaridades entre ellas que no pueden ser fruto de la casualidad, como sigue:

- a. El género no es considerado relevante por ninguna técnica "sin inconsistencias", como las que afloraron en el Análisis de Conglomerados, donde la variable género parecía ser el factor más relevante a la hora de crear los conglomerados y, sin embargo, no servía de criterio diferenciador a la hora de determinar los perfiles de los pacientes.
- b. La Edad y el Tipo de Artrosis son considerados relevantes sin inconsistencias "claras" tanto por ANOVA como por Regresión Logística, aunque al no cumplir con las hipótesis básicas del modelo hay que apelar a la "robustez" de cada técnica, mientras que dichas inconsistencias sí son claras en el caso del "Análisis de Conglomerados" y en el caso del Análisis

Factorial Discriminante, técnica esta última que ofrece un gráfico de correlaciones canónicas con regiones indiferenciadas y claramente superpuestas.

 c. Las Interacciones entre factores, las cuales sólo han sido utilizadas por ANOVA y Regresión Logística dan lugar a las mayores inconsistencias:

Todas las interacciones relacionadas con la variable Género son consideradas irrelevantes o no significativas por ANOVA, mientras que sí son consideradas relevantes por Regresión Logística.

Ocurre lo mismo con la interacción restante "Edad-Tipo de Artrosis", pero en sentido contrario, ANOVA la considera relevante, no así la Regresión Logística.

En nuestra muestra aleatoria el sexo no fue demostrado ser relevante. Esto podría ser debido a la aleatoriedad de la muestra, el hecho de que los pacientes son en su mayoría venía de una clase socioeconómica más alta (es decir: la mayoría de los pacientes optó por recibir el tratamiento en la clínica a sí mismos), y no enviados por el médico especialista.

Las distintas técnicas y métodos estadísticos empleados en esta tesis tienen diferentes características y debido a la falta de cumplimiento generalizada de las hipótesis de los modelos hay que recurrir al concepto de "Robustez" de las técnicas, es decir, a la consistencia en los resultados obtenidos con distintas muestras. Debido a que la hipótesis de Homocedasticidad es la que menos se ha cumplido en general, la técnica de Regresión Logística debiera ser la más robusta ya que no depende de la homocedasticidad de los residuos del modelo, y por ello debiera ofrecer los resultados más precisos y fiables.

Según la técnica de Regresión Logística la Edad y el Tipo de Artrosis son factores relevantes para explicar el grado de gravedad de la artrosis de cadera, con atención al efecto que el género tiene al interactuar con ellos.

CONCLUSIONES:

Existen varias investigaciones que no encontraron evidencias de que los datos demográficos de los pacientes con artrosis de cadera influyesen sobre la gravedad de ésta.

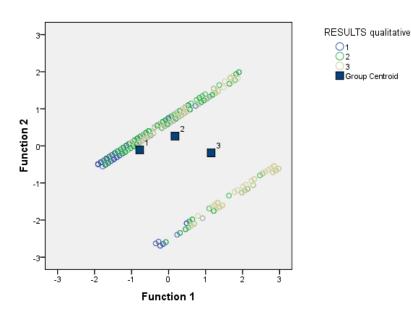
Algunos de los autores de estas investigaciones se quedaron completamente atónitos por este hecho y no pudieron encontrar ninguna explicación científica para ello. Por ejemplo, Byers, P. D. and Glennie, B., (1975) se refirieron a la osteoartritis como un "Espectro de Enfermedad" en el sentido de la complejidad de los factores envueltos en este tema.

Hay estudios más modernos que van en la misma línea de no encontrar consistencia en los resultados obtenidos respecto a los factores demográficos en relación a la gravedad de la Artrosis de Cadera, cabiendo citar los realizados por Birmingham, T. B., (2009) y Murphy, S. L. et al. (2011), con no menos sorpresa por su parte.

La tasa de acierto a la hora de clasificar a los pacientes de acuerdo a la técnica de Análisis Factorial Discriminante debería dar la misma cifra, en caso de haber realizado un análisis consistente con esta técnica, que la obtenida a través de Regresión Logística. Las diferencias pueden ser debidas a la falta de cumplimiento de las hipótesis básicas del modelo.

Tal inconsistencia en los Resultados obtenidos a través del Análisis Factorial Discriminante puede ser observada gráficamente ya que al representar la función de correlación canónica en unos ejes cartesianos las regiones A, B, C correspondientes a cada grado de gravedad de la coxartrosis se hallan superpuestas, haciéndose prácticamente irreconocibles:

Canonical Discriminant Functions



Estudios recientes como el realizado por Castaño Carou, A.I., (2014), han revisado la literatura existente sobre los factores que influyen sobre la incidencia de Artrosis de Cadera en la población, encontrando que el Género influía claramente sobre la misma, ya que las mujeres son más propensas a padecer esta enfermedad.

La edad también resultó relevante especialmente en el tramo comprendido entre los 70 y 79 años, donde se da un incremento exponencial en el número de casos, esta conclusión va en línea con nuestros hallazgos para la gravedad de la lesión, aunque nosotros no hemos estudiado la incidencia de la misma ya que todos los sujetos del estudio tenían ya artrosis de cadera.

En cuanto a la interaccción entre Edad y Género ésta resultaba relevante sobre la incidencia de la lesión, si bien en este estudio no se

realizaba ningún test para validar estas conlusiones, limitándose a la revisión de la literatura.

DIRECCIONES DE MEJORA:

El uso de Funciones Discriminantes "Cuadráticas" en lugar de las "Lineales", utilizadas en esta investigación, podría ayudar a mejorar la consistencia de los resultados obtenidos a través de la técnica del Análisis Factorial Discriminante, la cual ha clasificado erróneamente muchos de nuestros datos, alcanzando una tasa de éxito muy baja.

En relación a las mejoras en el análisis estadístico hay referencias en la literatura internacional acerca de este tema que sugieren el empleo de transformaciones logarítmicas en las variables explicativas para intentar lograr la Normalidad de los residuos del modelo.

Asimismo deberían usarse medias "geométricas" tras la transformación logarítmica de las variables, ya que las medias "aritméticas" ya no serían utilizables para obtener estimaciones eficientes y consistentes.

Nuestros datos poseen una gran asimetría y estas transformaciones logarítmicas podrían ayudar a mitigar dicha asimetría y a alcanzar algún tipo de Normalidad en los residuos del modelo.

Para poder medir la "Evolución" de la gravedad de la Artrosis de cadera se necesitarían mediciones en dos momentos distintos del tiempo.

Por la misma razón tampoco se ha podido determinar científicamente la eficiencia del tratamiento médico suministrado a todos los pacientes de la muestra en la cantidad de 7 sesiones, además de que el hecho de proporcionar el mismo número de tratamientos a todos los pacientes impide discriminar por este factor, convirtiendo la variable "número de tratamientos" en una constante o supuesto del modelo.

Asimismo los datos sobre "Nivel de No-Dolor" ofrecen demasiados valores repetidos, y no parecen tener una medición demasiado precisa, lo cual impide

que dicha variable se mueva libremente en el campo continuo, en el intervalo 0-100. A consecuencia de esto no se ha podido aplicar la técnica de "Regresión Lineal Multivariante" con variabledependiente cuantitativa, teniéndonos que conformar con la Regresión Logística Multivariante de variable dependiente categórica. Esta circunstancia ha podido influir también en la consistencia de los resultados obtenidos con ANOVA, técnica que utiliza también los valores cuantitativos de la variable "Resultados" o "Nivel de No-Dolor".

INTRODUCTION:

An anatomical study appeared recently in the American Journal of **Sports Medicine** identifying for the first time the cross sectional anatomy of the iliopsoas at the level of the acetabular labrum by Alpert, J.M., et al., (2010). The study emphasized the fact that until recently the iliopsoas (or iliopsoas tendon) was not readily identified or emphasized as a possible cause of hip damage¹ that ultimately results in the need for hip replacement. The tight or shortened iliopsoas can cause an increase in intra-articular pressure with a resultant hip degeneration pain syndrome including, irritation of the synovial bursa, snapping hip and faulty displacement of the leg which in itself can cause a chain reaction of further problems in the knee and foot (which is beyond the scope of this thesis). The increase in hip intra-articular pressure may result in a cascade of negative effects in the hip joint which ultimately results in a loss of cartilage in this joint and this fact may lead to pain, loss of movement, etc. At this point and with no treatment is it possible for the femur head to break through the thinning structures of the acetabulum of the pelvis with potential life threatening complications?

A literary review on the subject of the influence of the local muscles over the stability of the hip (Retchford, T.H., Crossley, K.M., Grimaldi, A., Kemp, J.L., Cowan, S.M., 2013) has been published on an australian medicine journal (**Journal of Musculoskeletal and Neuronal Interaction**) in 2013. According to last findings on this relationship between muscles that surround the hip and the hip inself based on the known characteristics of local muscles and the limited research available on hip muscles it is proposed that the local hip muscles (quadratus femoris, gluteus minimus, gemelli, obturator internus and externus, iliocapsularis and the deep fibres of **iliopsoas**), may be primary stabilisers of the hip joint. Therefore, interventions aimed at restoring isolated neuromuscular

¹ In reality there was a research dated 1962 which can be considered a pioneer of this matter. On this research Arthur A. Michele (Michele, A. (1962) considers many pathological processes occurring in the hip joint and the lumbar spine, and associates these changes with the action of the iliopsoas. If this muscle is powerful enough to create various disabilities of the hip and spine, it is hard to see that in man it is a vanishing muscle. It is significant that the autor considers that the active contraction of both iliopsoas muscles is equivalent to the pull of more than a ton in weight.

function of the primary hip stabilisers may be considered when treating people with passive hip instability prior to commencing global muscle rehabilitation. Whilst the hip joint is considered to be stable due to its bony architecture and strong capsuloligamentous restraints, evidence suggests that deficits in the acetabular labrum and iliofemoral ligaments may lead to increased femoral head translation and possibly to early degenerative hip pathology (DDH).

The article keeps saying that some sports like gymnastics, football, tennis, ballet, martial arts.....and golf may influence the development of focal laxity. Active stability of the hip joint from tension in hip muscles may augment passive stability in the normal and structurally abnormal hip.

The article of the australian research team finally says:

[...."Despite this likely important role, little is known about what muscle or muscle synergies are involved or if hip pathology has an influence on hip muscle function"...]

Hip degeneration was always thought to be idiopathic in nature and was never in the medical community considered to be a disease process that could be altered or stopped. This lack of knowledge of the iliopsoas connection to hip degeneration is now only beginning to become known - as a result there has been much unneeded suffering, operations, loss of mobility and resulting general loss of health in many people over the years. Through this thesis we hope to further develop the knowledge of this disease process with case studies to show the possibility of stopping this disease process. The loss of mobility associated with iliopsoatic syndromes, and subsequent hip degeneration, not only affects the hip and leg, it may have a general negative effect on the overall health status of the patient. As the patient reduces activity there is an accompanying reduction in overall fitness, decrease in metabolic function (possible future **metabolic syndrome**), decrease in neurotransmitter activity in the brain (possible **depression**), decrease in work output, loss of employment, social breakdown, etc. With the simple identification of pathological shortening

of the iliopsoas can many of these diseases and social processes be stopped or avoided. This is something that the medical community has not pursued and as a result the resulting costs on society have soared in the last years with the possibility that the demand for this procedure will be greater than the availability of orthopaedic surgeons to perform this procedure in the aging (and sitting, thus more iliopsoas shortening) baby boomer population. Through the simple evaluation and treatment methods that will be discussed later in this thesis it can be shown that there can be a very large and beneficial impact on the public health sector. The present knowledge in the year 2014 of this subject is not at the level it should because the gatekeepers of this information are also the ones who benefit by not promoting preventative research.

3 CHAPTER I

3.1 BACKGROUND:

As a result of systematic searches on the subject of *iliopsoas* and *hip arthrosis*, and other attempts, in *PubMed*, the query tool for the *MedLine* Data Base, the following documents were found that could be suitable as background for the current thesis:

Alpert, J.M., et al. (2010). Cross-Sectional Analysis of the Iliopsoas <u>Tendon and Its Relationship to the Acetabular Labrum. Boston:</u> <u>The American Journal of Sports Medicine:</u>

This article is the milestone for the present dissertation since they were pioneers at finding the relationship between the iliopsoas and the acetabular labrum.

Retchford, T.H., Crossley, K.M., Grimaldi, A., Kemp, J.L., Cowan, S.M. (2013). Can local muscles augment stability in the hip? Melbourne: Journal of Musculoskeletical and Neuronal Interaction:

This article provides a very wide literary review of more than 100 researches about the subject that we try to develop along the present dissertation.

Akgül, T., Bora Göksan, S. and Eren, I.(2014). Idiopathic hypertonicity as a cause of stiffness after surgery for developmental dysplasia of the hip. International Journal of Surgery:

This research offers a very interesting study case about the relationship between diseases of the hip and the iliopsoas muscle:

Van Den Berg M., Castellote J.M, Mahillo-Fernandez, I. (2012). Incidence of Nontraumatic Spinal Cord Injury: A Spanish Cohort Study (1972–2008). Archives of Physical Medicine and Rehabilitation.Vol. 93 Nº 2. Elsevier:

This article is very interesting since provides a study of the incidence of non-traumatic spinal cord injury among Spanish population and the Asia Impairment Scale is described, which can be worthy for our purposes.

<u>Gómez-Ferrer Sapiña, R. (2005). Estudio biomecánico de la marcha</u> <u>en pacientes con artrosis de cadera. Tesis Doctoral. Valencia:</u> <u>Universitat de Valencia</u>:

This thesis links some biomechanical features of gait to the existence of monolateral hip arthrosis and it has an interesting methodology that could be useful for our Research.

Mendis Dilani, M. et al. (2014). Hip flexor muscle size, strength and recruitment pattern in patients with acetabular labral tears compared to healthy controls. Australia: Elsevier:

[.... "Acetabular labral tears are a source of hip pain and are considered to be a precursor to hip osteoarthritis. Hip flexor muscles contribute to hip joint stability and function but it is unknown if their size and function is altered in the presence of labral pathology"....]

This article contains very updated information that seems to go in the same direction that our research.

Alfred Baring Garrod (1848). Observations on the blood and urine of gout, rheumatism and Bright's disease. London: Medical Chirurgical Transactions :

This article is a classic and the author can be considered a pioneer in the study of arthrosis.

Alfred Baring Garrod (1859). Treatise on nature and treatment of gout and rheumatic gout. London: Walton and Maberly:

This is the first time in which the expression osteo-arthritis is used

3.2 PURPOSE OF WORK:

As the active large "baby boomer" generation reaches the 60 years old age levels and older the present amount of orthopedic surgeons will not be enough to meet the demand for hip replacements in this group. As such a new model is needed at this time to stop hip degeneration before it reaches a point that the hip needs to be replaced. This paper presents information that may be helpful in reaching this goal.

3.3 GLOBAL OVERVIEW²:

3.3.1 The Most Important Muscle Syndrome

² **Note**: For anatomic support of the text we will use the series of atlas of anatomy of Frank H. Netter

The iliopsoas, one of the major muscle complexes of the body, is the key to most cases of muscle imbalance. It goes from the spine through the abdomen and over the brim of the pelvis to the inner part of the upper thigh. Its normal function is involved with the entire working of the back, the hip, and the pelvic area.

The Iliopsoas is one of the main controllers of posture in the body, because the iliopsoas affects movement of the body in such a wide area, it is primary source of most muscle imbalance; even through other muscles may also be functioning improperly. If iliopsoas is shortening it could pull everything else out of kilter and it could cause a person to be round-shouldered, have a slumped posture, or swayback. When the contracted iliopsoas pull on the femur-the thigh bone-where it attaches at the hip, the abnormal strain on the thigh bone causes the upper leg to rotate outwards. The lower leg turns also to compensate, twisting the two lower leg bones-the tibia and fibula-out of the proper relationship. The pulling produces a torsion effect, an outwards twisting. Such torque or twisting could produce the pain on the inside of the knee and outer hip and thigh. This torsion may also prevent the foot from resting squarely on the ground. The resulting rolling of the foot during walking creates another source of stress and pain.

They can also be too short on just one side. Then it will throw things out of kilter on one side and will cause many of the muscles on both sides of the body to change this way and that in compensation for the one-sided pull.

The iliopsoas is just one muscle, but it affects a whole network of other muscles. The iliopsoas muscles are interdependent, like the rowers in a crew race.

If the iliopsoas muscle contracted, all of the other muscles on the team must work too hard to compensate so that there is a constant possibility of strain at every point.

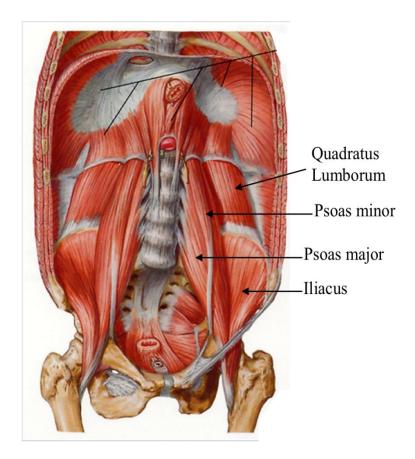


Figure 1.Anatomy of iliopsoas muscle

3.3.1.1 lliopsoas

The term **iliopsoas** refers to the combination of the psoas major and the iliacus at their inferior ends, as we can see on Figure 1. These muscles are distinct in the abdomen, but usually indistinguishable in the thigh. As such, they are usually given the common name "iliopsoas" and are referred to as the "dorsal hip muscles" or "inner hip muscles". The psoas minor does not contribute to the iliopsoas muscle.

It comprises a complex of two muscles with different areas of origin. This muscle belongs to the striated musculature and the innervation is carried by the femoral nerve as well as direct branches of the lumbar plexus. The iliopsoas muscle consists of: a) Psoas major muscle: originates from the 1st to 4th lumbar vertebrae, the costal processes of all lumbar vertebrae and the 12th thoracic vertebrae and inserts at the lesser trochanter of the femur.

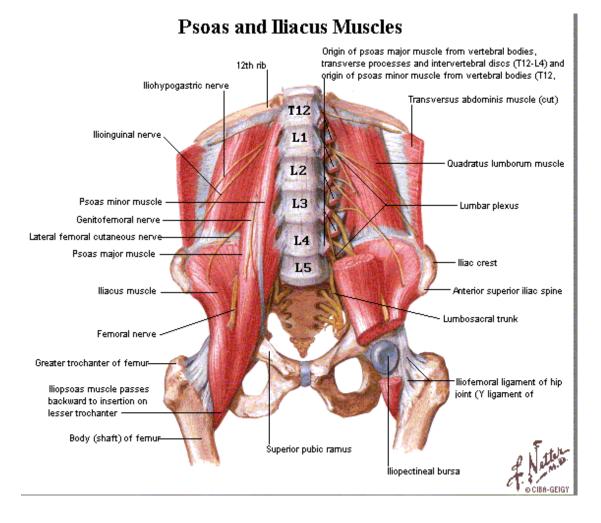


Figure 2.Insertion of the iliopsoas muscle in the spine

 b) Iliacus muscle: runs from the iliac fossa to the lesser trochanter. The psoas major and iliacus muscle unify in the lateral pelvis shortly before the inguinal ligament becoming the iliopsoas muscle. There they pass below the inguinal ligament through the muscular lacuna together with the femoral nerve. Both muscles are completely surrounded by the iliac fascia. The lumbar plexus lies dorsally from the psoas major muscle which is penetrated by the genito-femoral nerve. Medially from the psoas major runs the sympathetic trunk.

3.3.1.2 Origin

The psoas major originates along the lateral surfaces of the vertebral bodies of T12 and L1-L5, as it can be seen on figure 2, and their associated intervertebral discs. The iliacus originates in the iliac fossa of the pelvis.

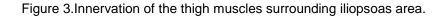
3.3.1.3 Insertion

The psoas major unites with the iliacus at the level of the inguinal ligament and crosses the hip joint to insert on the lesser trochanter of the femur. The iliopsoas is involved in flexion and lateral rotation (supination) of the thigh. If the limb is fixed they involve in flexion of the trunk.

3.3.1.4 Innervation

The psoas major is innervated by direct branches of the anterior rami off the lumbar plexus at the levels of L2-L4, while the iliacus is innervated by the femoral nerve (which is composed of nerves from the anterior rami of L2-L4).

Muscle	Origin	Insertion	Innervation	Blood Supply	Action
lliopsoas/psoas major	Sides of vertebra T12 to L5 and transverse processes of L1-L5	Lesser trochanter of femur	Ventral rami of lumbar spinal nerves 1-3	Lumbar branches of iliolumbar artery	Flexes thigh at hip and stabilizes the hip
lliacus	lliac crest, iliac fossa, ala of scrum, and anterior sacroiliac ligaments	Tendon of psoas major and body of femur, inferior to lesser trochanter		lliac branches of iliolumbar artery	Flexes thigh at hip and stabilizes the hip
Tensor fasciae latae	Anterior superior iliac spine and anterior part of external lip of iliac crest	lliotibial tract → lateral condyle of tibia		Superior gluteal arteries, lateral circumflex femoral artery	Abducts, medially rotates and flexes the thigh, stabilizes trunk on thigh
Sartorius	ASIS and superior part of notch below it	Superior part of medial surface of tibia	Femoral nerve (L2-L3)	Femoral artery	Abducts, laterally rotates and flexes the thigh
Quadratus femoris	Lateral margin of ischial tuberosity	Quadrate tubercle on intertrochanteric crest	Nerve to quadratus femoris	Medial circumflex femoral artery	Laterally rotates thigh



3.3.1.5 Properties

The iliopsoas muscle is the strongest flexor of the hip joint (important walking muscle). In the supine position it decisively supports the straightening of the upper body (e.g. during sit-ups). Furthermore it rotates the thigh laterally. A unilateral contraction leads to a lateral flexion of the lumbar vertebrae column. Altogether the iliopsoas muscle plays a significant role in the movement and stabilization of the pelvis.

The iliopsoas is the strongest of the hip flexors (others are rectus femoris, sartoriu, and tensor fasciae lat). The iliopsoas is important for standing, walking, and running. The iliacus and psoas major perform different actions when postural changes occur.

It is, however, a typical posture muscle dominated by slowtwitch red type 1 fibers, known as oxidative fibers due to the fact that they produce ATP (Adenosine Triphosphate) through intake of oxygen. These fibers have been built for slow but enduring movement. Therefore, it is susceptible to pathological shortening or contracture, especially in older people with a sedentary lifestyle, and requires regular stretching to maintain normal tone. Such shortening can lead to increased anterior pelvic tilt and lumbar lordosis (unilateral shortening), and limitation of hip extension (bilateral weakness).

The iliopsoas muscle is covered by the iliopsoas fascia, which begins as a strong tube-shaped psoas fascia, which surround the psoas major muscle as it passes under the medial arcuate ligament. Together with the iliac fascia, it continues down to the inguinal ligament where it forms the iliopectineal arch which separates the muscular and vascular lacunae.



Figure 4.Anatomy of iliopsoas muscle and surrounding bones

3.3.2 Anthropology

3.3.2.1 Prehuman Ancestors

The earliest ground-living prehumans' ancestors were four feet high, the arm did not present the characteristics of the anthropoid apes. The head was thrust forward and the flexible spine was a simple anteroposterior rounded curve, the lumbar spine was flat, the knees were slightly flexed. Their postural habits alternated between short standing, rapid running and squatting. This is the signs of shortened iliopsoas.

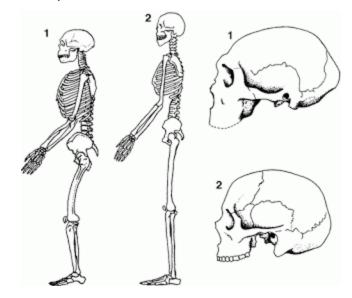


Figure 5.Comparison of bone structure between human being and first ancestor

3.3.2.2 Anthropoidea

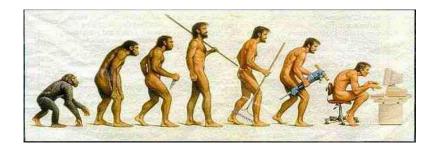


Figure 6.Anthropoidea families

Anthropoidea are divided into five families, three of monkeys, one of apes and one of man. It is a suborder of the mammalian order Primates, which comprises the families Cebidae (New World monkeys), Callithricidae (marmosets), Cercopithecidae (Old World monkeys), Pongidae (gibbons, gorillas, chimpanzees, and orangutans), and Hominidae (humans)³.

The apes' vertebral column presents a uniform curve, while man by reasons of the action of the iliopsoas, has developed a secondary or compensatory curve through reversal of curves or lordosis of the lumbar and cervical regions.

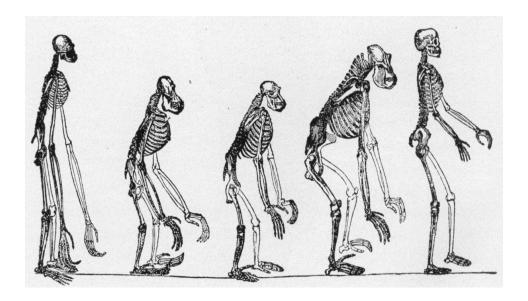


Figure 7.Skeletons of Gibbon, Orangutan, Chimpanzee, Gorilla and Man

3.3.2.3 The Erect Posture as a Factor in Production of Anomalies in Man specifically in the hip joints

Becoming erect on the ground was a critical stage in human evolution and a prerequisite to the final stages in human cerebral evolution ⁴(Weidenreich, M., 1913).

³ Farlex Partner Medical Dictionary (2012)

⁴ Weidenreich discovered and described the initial findings of Sinanthropus, now classified as Homo Erectus. He went to China in the midthirties and resumed the work of Davidson Black at Zhoukoudian. Because the Sinanthropus originals disappeared during World War II,

When man assumes his unique posture of lumbar lordosis, a necessary adaptive elongation of the lliopsoas must take place.

Once the abnormal force is in operation, it is a contributor to the formation of lesions of the hip, such as developmental dislocation; dislocation of the hip and torsion fractures of the neck of the femur.

Persistence of the abnormal tension is contributory to deformation of various structures, the direction influenced by the origin or insertion of the lliopsoas.

A complete understanding of the development of posture and formation of the ilipsoatic force lights the way for a rational approach to treatment of the aforementioned pathologies, by conservative stretching and exercise of muscles involved, converting the force from an agent of destruction to one of stabilization.

3.3.3 The lliopsoas Imbalance

3.3.3.1 In the beginning: causes of muscles imbalance

The muscle system starts forming and growing when the tiny human embryo is still in its mother's womb, barely more than a worm bathed in the cushioning and nourishing liquid, growing into the patterns that make up the human body.

3.3.3.2 The Crucial Years

Weidenreich's descriptions and the casts prepared under his advice provided the only traces left of these famous hominid fossils

Many cases of imbalance seem to originate during childhood and adolescence. At birth all the muscles and bones of the adult human are present, but they still have much growing to do. The long bones, such as those of the legs and arms, grow by forming new cartilage where the shaft of the bone meets the head. As this cartilage hardens to bone and new cartilage is formed, the bone becomes longer and longer. Finally in the adult the long shaft and rounded head unite and the entire bone is firmly and permanently hardened.

The curve of the spine changes too. In the embryo the spinal column is shaped like a shallow letter C. In the embryo the curve starts to change and the curve continues to change as the child grows, until it resembles an elongated S in the adolescent. This is the normal curvature of the spine. It appears in stages. The first curve develops in the neck region, about when the infant tries to expand his horizon of vision and holds his head more erect. The second curve in the small of the back, the lumbar region, starts to form when the child begins to sit up, develops further when he begins to creep, and it is almost completely developed by the time he stands.

The first seven years of life is the period of most rapid growth. This is a particularly vulnerable period. If the muscles keep up with bone length there are no problems. During the elevation of the center pole of a circus tent, if one of the ropes is short it will deflect the pole toward the shortened rope. During the period of most rapid growth, if any of the muscles fails to elongate with rapid skeletal growth, the spine, leg, or arm bones will deflect toward the shortened muscle and a cycle of muscle imbalance commences. And if the child has a muscle problem, this is the time to find and correct it before permanent hardening of the bones takes place, when symptoms become more disruptive and harder to treat.

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During these critical first years of skeletal development, and during the growth spurt of adolescence, the skeleton is under much stress and is dangerously vulnerable to development of abnormalities.

3.3.3.3 From Ape to Modern Man-The Key

Erect posture freed man's hands for work, but standing erect may also have given him much of the back trouble and other posture problems that afflict him today.

Charles Darwin⁵, whose observations led him to postulate the theory of evolution, used the phases "**natural selection**" and "**Preservation of Favoured Races in the Struggle for Life**" to describe this process:

> [...." Owing to this struggle for life, any variation, however slight and from whatever cause proceeding, if it be in any degree profitable to an individual of any species, in its infinitely complex relations to other organic beings and to external nature, will tend to the preservation of that individual, and will generally be inherited by its offspring. The offspring, also, will thus have a better chance of surviving, for, of the many individuals of any species which are periodically born, but a small number can survive"....]

It is believed that our earliest prehuman ancestor had long dangling arms and often dropped down on all fours and scampered along, or squatted with his hands touching the

⁵ Charles Darwin published in 1859 his main work with the title of "On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life", which was changed later to a shorter title, "To the origin of Species", for simplification purposes.

earth. His head was large and heavy, bent thrust forward on a short neck to almost touch his chest. His spine was almost straight. Although his legs could be completely extended, the knees were usually kept partly flexed, not unlike the knee of a chimpanzee.

But as man became more upright, his whole geometry and anatomy changed. Compare the skeletons of Neanderthal man and modern man shown below.

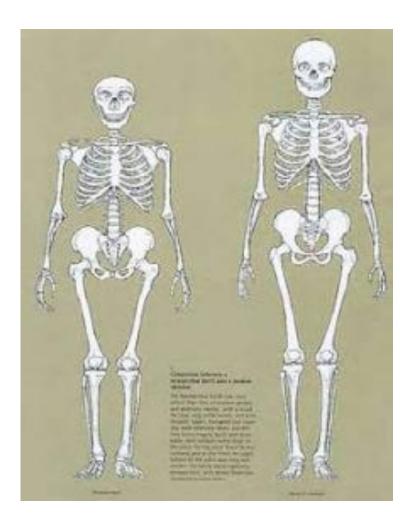


Figure 8.Neanderthal man on the left, modern man on right

Modern man's head is poised delicately on his straight neck instead of thrusting forward. Eventually his legs became

completely straight instead of bent and bowed. His pelvis broadened and the leg bones flared out to support the weight of this upright man. In compensation for all the weight and posture changes, the spine became curved in a shallow S-shape.

Muscles as well as bones underwent adaptations to hold man upright. Muscle attachments shifted to different parts of the bones to compensate for the different movements required for twolegged walking. The calf muscle developed extensively, making it possible for the knee to be fully extended and straightened instead of always flexed as if crouching, and the powerful gluteus maximus, the muscle in your seat, made it possible for the hip joint to straighten out in the same way.

As a consequence, some of the greatest muscle changes took place in the iliopsoas muscle. Over the ages, as man gradually assumed his upright position, the iliopsoas underwent considerable strengthening and elongation. Technically speaking, the points of origin and insertion of the iliopsoas gradually increases and the muscle became progressively stouter in order to support and stabilize the upright posture.

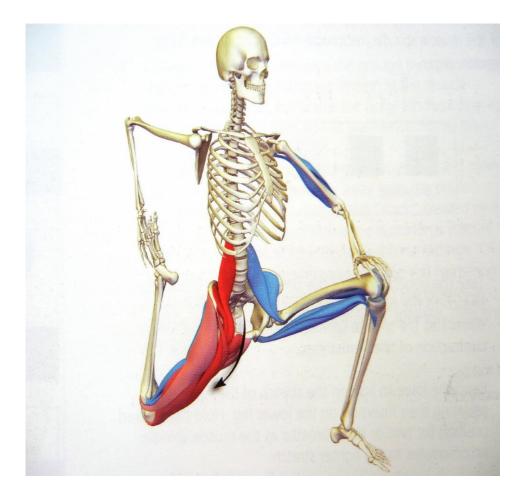


Figure 9. Influence of the iliopsoas on, and suitable stretching of, the surrounding areas

But the evolution of the iliopsoas has not been uniform in all human beings. For some reason, many people have an iliopsoas too short. It is not elongated and flexible as it is in most people and as it should be. Instead, it has reminded short and rigid, pulling against bones and joints creating constant tension. For individuals who have this defect to maintain an erect posture, some 1300 pounds of tension, following Michele, A.,(1962), pulls on their spines and thigh bones. This puts tremendous stress on the hips, constant wear and tear on the back and knees, and eventually can contribute to deformities of the spine, pelvis, and hips. It may also secondarily cause muscle imbalance in the legs, ankles, and feet. As muscle tension continues and spreads, there can even be permanent injury to bones and joints, or such extremely poor posture as to injury internal organs. This imbalance of the iliopsoas is a sort of evolutionary "hangover", in which a third of humanity still does not have this particular advantageous structural change. In a way, it is proof that the evolutionary process, as Charles Darwin would say, is still going on.

3.3.4 How the Bones and Muscles work

To understand muscle imbalance, and to understand how exercise and other treatments can help, you first need to understand the normal structure and motion systems (kinesiomechanics) of the body. If we know how our muscles and bones work normally, then we will better understand what happens when they are not working normally.

3.3.4.1 The Body's Engineering System

What is the physiology of motion? What are the forces and actions that allow us to walk and reach and turn and hold on to things? How do our muscles and bones act together to establish such perfectly balanced forces that we are stabilized and in equilibrium, that we don't fall on our noses or trip over our feet?

The anatomy of our musculoskeletal system is relatively simple to understand. The muscles contract and relax and act as springs and pulleys, moving bones up and down, back and forth. The bones are the levers, and the joints are the fulcrums of pivot points about which the bones move. How and where a muscle is attached to a bone, the shape of the muscle, the shape of the bone it is attached to, and the kind of joint involved, all of these determine what kind of action will result from the contracting and relaxing of a certain muscle.

When the muscles are in normal balance, they make the body work smoothly; when they are out of balance, there is stress and strain of the joints. It's all a matter of the basic principles of physics.

Figure 10.Lower Limb like a physical system. Source: Anatomy of Gray (Gray, H.(1918))

3.3.4.2 Kind of Joints

There are several types of joints. Bones can be joined together in a way that allows them to move, or in a way that stabilizes them.

A hinge joint, like the hinge on a door or a trunk lid, allows the muscle to pull the bone in only one direction. The knee joint is a good example. We can bend the knee or straighten it, but we can't bend it backward (hyperextend) or rotate it or move it in any other direction.

A **saddle joint** is shaped somewhat like a western saddle with two ends tipped up making hollows in the surfaces in both directions. This allows forward and backward as well as sideways movement. An example is a thumb joint, where the bone at the base of the thumb is attached to the bone of the hand. Another is the hind foot, the joint between the talus and the calcaneus. Abnormal deflection of this joint inward results in what is called a varus heel, while an outward deflection results in a valgus heel (**flat foot**).

A **ball-and-socket joint** allows the round head of one bone to fit into the socket of the other bone, like the swivel joint on the top of a camera tripod. It permits bending, straightening, forward or backward motion, or rotation-just about any kind of movement you may want to make. Examples are the shoulder and hip joints.

Still **another kind of joint** connects the vertebra in the spinal column. The vertebrae are joined together by cartilage that touches and connects each vertebra to the next. The result is a supple chain that allows the motion of twisting and bending.

3.3.4.3 What is a Muscle? What Does It Do?

A muscle is made up of tiny fibers or cells, each stretching the length of a bundle of muscle tissue like a thin thread. These fibers are joined to make larger bundles, until a complete mass of muscle is formed. Each of the long skinny cells is capable of contracting when stimulated by a nerve impulse. And when a group of muscle fibers contracts, the muscle mass they make up contracts and shortens.

The attachment of a muscle determines what kind of work that particular muscle will have to perform. Muscles and their attachments determine the positions and movements of all the various parts of the body in relation to each other.

If you looked at a piece of muscle under a microscope, you would see that each bit of muscle is made up of a bundle of fibers, each about the thickness of a human hair. But each hair-thin fiber can support as much as a thousand times its own weight. There are about 6 billion of these tiny muscle fibers in our body.

If you were to examine many muscle fibers under the microscope, you would notice that there are three kinds. One has light and dark stripe like bands across the sheathed fibers and is variously called striped muscle or skeletal muscle (because it is attached to bones of the skeleton) or voluntary muscle (because it is used for voluntary movements such as throwing a ball or walking).

A second kind of muscle fibers is smooth and not striped. It is called involuntary and rules the work of all the internal organs (except the heart). It controls such things as breathing, stomach action and intestinal movements.

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The heart has the third type of muscle, called cardiac muscle. These fibers are striped, but are not separated from each other by sheaths as the skeletal muscles are. Instead they are joined in a continuous network. The heart muscle is also involuntary muscle, operating without a signal from the brain.

There are two entirely different nervous systems for the voluntary and involuntary muscle systems. In the case of the voluntary muscles, the signal is sent from the brain through the *central nervous system.* The split-second signal races along nerves from the brain to the spinal cord, where the signal is relayed to another nerve that shoots it to the proper muscle fibers. Thus stimulated into action, the fibers all contract simultaneously, becoming almost a third shorter and correspondingly thicker.

The smooth involuntary muscles, however, receive their signals from a different set of nerves- the *autonomic nervous system*. They are "automatic" and do not need to be "thought" about and directed. These nerves originate in a different part of the brain. They are divided into two subsystems: The sympathetic nervous system and the parasympathetic. The sympathetic dilates the pupils of the eyes; the parasympathetic slow it down.

3.3.4.4 Muscle Attachments

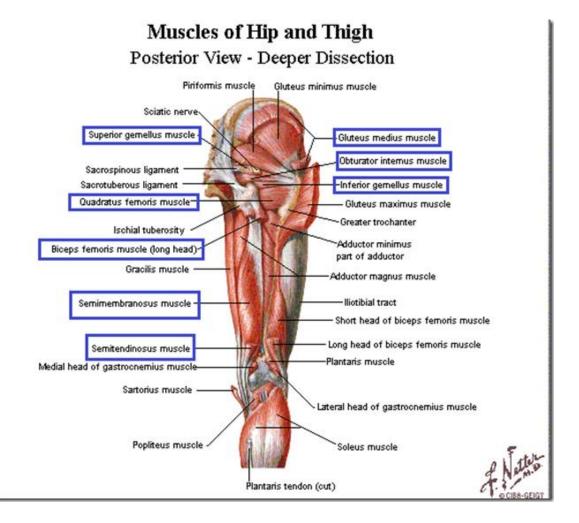


Figure 11. Muscles of Hip and Thigh

Muscles also differ in how they are attached.

The muscle is stimulated by a signal from the spinal nerves going to it. The muscle fibers contract, pulling on both bones that the muscle is attached to. Theoretically, both bones should move, since the tension is in the middle and pulling both of them. But usually one bone or the other is stabilized, held motionless by other muscles, so just one of the bones will move when the muscle contracts. If you kick your leg out, the upper of your leg remains still. Only the lower leg moves out when the big muscle contracts.

The point where the muscle is attached to another bone that holds steady is called the **origin**. The point where the muscle attaches to the bone that moves is called the *insertion*.

So what a muscle does whether it flexes a leg or extends it, whether it moves a bone up or down, backwards or forwards, or causes it to rotate. All depends on where the muscle is attached, how it pulls, and how the joint let the bone move.

This explanation is oversimplified. Most muscles have many attachments, and many muscles work together or against each other. And some muscles simply act as stabilizers, steadying and supporting various parts of the body.

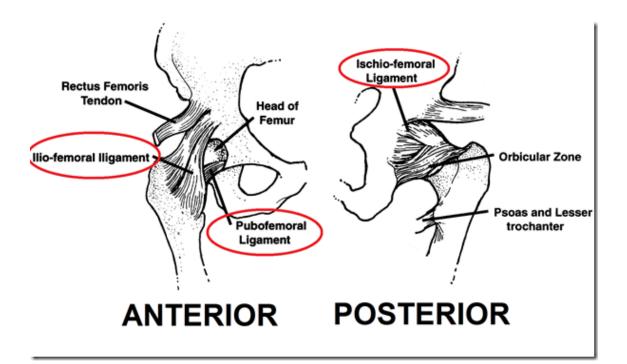


Figure 12. Anterior and Posterior View of Hip Joint

Some act as brakes, to keep the most powerful muscles from moving a bone too far. And still other muscles are more or less "emergency muscles", giving help to other muscles when extra force is necessary or when they have to act against resistance.

Usually muscles are at least paired in their action. That is, for one muscle that causes the arm to flex, there is at least one muscle that does just the opposite, making the arm extend. So when one muscle contracts, another one must relax. In fact, the nervous system is set up with an elaborate switching system so that when a nerve impulse goes to its opposite action muscle to inhibit its contraction and cause it to relax.

Some muscles extend over two or more joints, so other sets of muscles also become involved when they act.

3.3.4.5 One Muscle Can Affect Your Entire Body

By now we are aware of how muscles interact. When we realize that muscles may be attached to as many as a dozen different bones as well as to other muscles, we can begin to understand how one muscle can affect many parts of your body. And we can realize how one muscle's being too short, too rigid, too weak, or otherwise improperly balanced in relation to other muscles can upset the functioning of the other muscles. As one muscle functions abnormally, other muscles all down the line must compensate and make adjustments.

Sometimes you can actually feel your muscles pulling in their many ways, interconnecting in their complex systems throughout your body. If we stretch our arms high while standing

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on your toes for a long time, as when putting things on a high shelf or wallpapering a ceiling, we can feel those muscles pull right from our fingertips down through our shoulders, our back, and down into your hips and legs, and even into our hips and legs, and even into our straining arches and toes.

The iliopsoas muscle is especially important because it interacts with and influences so many other muscles and parts of the body. The iliopsoas is mainly a broad flat muscle in the lower back, but like an octopus, it has arms reaching out in many directions. It has segments that go to every vertebra in the low thoracic (chest) and lumbar (back) areas of the spinal column, and other segments that go to the pelvic and thigh bones. It pulls in many directions, and it is powerful. In its normal function it makes the thigh move forward as well as rotate outwards from the spine and controls the pelvic tilt and general posture.

Abnormal functioning of this one major muscle can have ramifications reaching through a kinetic chain reaction up to the back of the neck down to the big toe. There are other important muscle systems as well, in addition to the iliopsoas, all with their own interrelationships and interconnections, and with their own symptoms when something goes wrong. But none of these other muscle systems can compare with or match the overall dominance of the iliopsoas muscle.

Because there are so many interconnections, it sometimes takes a while to find out which muscle is causing a person's problems. Because so many different muscles may be compensating, in order to determine which one is primarily at fault, it may be necessary to relax the muscles in that system one by one. But in regardless of this most problems lead back or originate in or from the iliopsoas.

Thus it may be discovered that a painful back is not really a bad back at all, but a referred symptom of improper functioning of the spino-pelvo-femoral muscles (thus the iliopsoas) of the hip. And pain in the hip is frequently originating to due to the fact that the iliopsoas muscle going to it is so rigid that the thigh bone (femur) can't rotate properly without grinding in the hip socket and eventually destroying this joint.

To illustrate this we consider interesting to describe one real case of a three years old child with Idiopathic hypertonicity as a cause of stiffness after surgery for **developmental dysplasia of the hip** (DDH) (Akgül, T., Bora Göksan, S. and Eren, I. (2014)) :

PRESENTATION OF CASE

[.... "Three-year-old patient referred to our institution with bilateral DDH. Two hips were operated separately in one year with anterior open reduction, femoral shortening osteotomy. Third month after last surgery, limited right hip range of motion and limb length discrepancy identified. Clinical examination revealed that patient had limited range of motion (ROM) in the right hip and compensated this with pelvis obliquity. Gluteus medius, sartorius and iliofemoral band release performed after examination under general anesthesia. Symptoms were persisted at 3rd week control and examination of the patient in general anesthesia revealed full ROM without increased tension. For the identified hypertonicity, ultrasound guided 100 IU botulinum toxin A injection performed to abductor group and iliopsoas muscles. Five months later, no flexor or abductor tension observed, and there was no pelvic obliquity.

DISCUSSION

Stiffness as a complication is rare and is usually resolved without treatment or simple physical therapy. Usually it is related with immobilization or surgery associated joint contracture, and

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spontaneous recovery reported. Presented case is diagnosed as hip stiffness due to underlying local hypertonicity. That is resolved with anesthesia and it was treated after using botulinum toxin A injection.

CONCLUSION

Hypertonicity with hip stiffness after surgical treatment of DDH differs from spontaneous recovering hip range of motion limitation and treatment can only be achieved by reduction of the muscle hypertonicity by neuromuscular junction blockage"....]

3.3.5 Physical Properties of the Pelvis, Sacro-iliac and Hip Joint the bridge between the upper and lower body

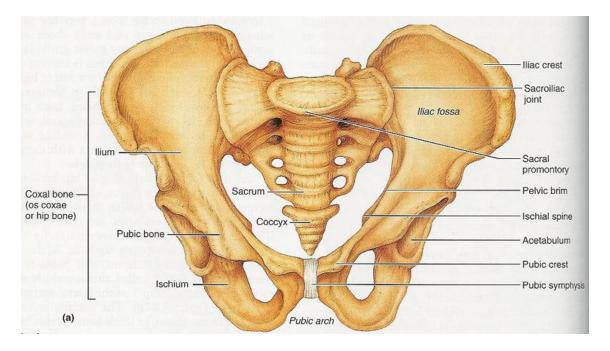


Figure 13.View of the pelvis

3.3.5.1 Orientation of the pelvis

In the so-called neutral position of the pelvis the anteroposterior iliac spine and the top of the symphysis are in a vertical plane.

It's apparent that the weight transmitted to the sacrum by the superincumbent vertebral column will press the upper end to rotate forwards and its lower end, including the coccyx, to rotate backwards. The ligamentous structures will resist this tendency to rotation.

3.3.5.2 Movement of the Pelvis

The sacrum rotates backwards and forwards between the hip joints. The pelvic interposition is situated between the mobile and immobile portions of the spine.

3.3.5.3 The Sacroiliac Articulation

The strong joint between the sacrum and the ilium is a synchondrosis, and through it the whole body weight is transmitted, the weight of the spine being passed to the pelvis and then to the leg.

Movement in the sacroiliac joint takes place around two axes, a transverse axis passing through the body of the second sacral vertebra, and a sagittal axis passing through the midpoint of the symphysis publis. Experimental data on the rage of movement confirmed that it was very small.

3.3.5.4 Physical Properties of the Hip joint

The hip joint is a multiaxial or ball-and-socket joint. It has three degrees of freedom of motion because it permits movement in three planes; a frontal, a sagittal and a transverse plane.

3.3.5.5 Position of the Acetabulum and Femoral Head

The position of the acetabulum is forward, lateral and downward. The head of the femur represents two-thirds of a sphere and is directed medially, upward and backward. The atmospheric pressure holding the head in the socket is amply capable of carrying the weight of the entire limb without ligamentous or muscular assistance. The Iliopsoas, femoral vessels and nerves pass from the pelvis underneath the inguinal ligament.

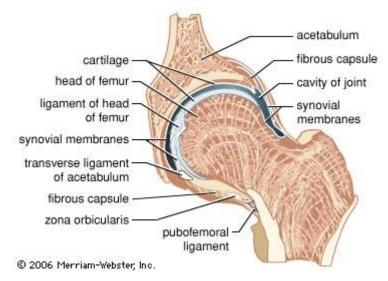


Figure 14.View of the Acetabulum and Femoral Head

3.3.5.6 Position of the Femoral Neck

The neck of the femur is pyramidal and obliquely placed. The roughness, called the trochanteric line, is due to the attachment of the massive iliofemoral ligament and, to the aponeurosis of the vastus medialis.

The neck is buttressed below by a rounded, strengthening bar that ascends from the lesser trochanter.

The lesser trochanter is the traction epiphysis of the lliopsoas. It is conical; it projects from the posterior surface of the bone and points medially.

The greater trochanter is the traction epiphysis of the gluteus medius and gluteus minimus. Its anterior and lateral aspects would be continuous with the corresponding aspects of the shafts but for the presence of a rough line that marks the site of fusion of the trochanter and shaft. A quadrate tubercle marks the site where the epiphyseal line crosses the intertrochanteric crest.

The contours of the femoral shaft are irregular. In the frontal plane the shaft shows an outward curve involving the head, neck and upper end of the shaft; in the sagittal plane the entire length presents a mild forward curve.

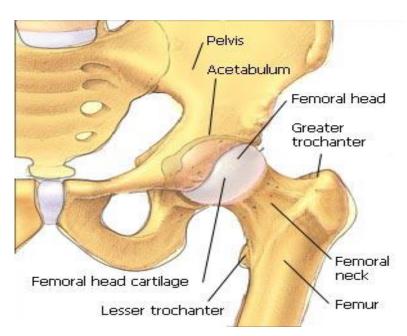


Figure 15. View of Femur Bone and its insertion in Hip Joint

Two principal trabecular systems reflect the static functions of the femur; a medial one from the medial cortex is the real weight-bearing system; a lateral one from the outer cortex crosses the former at right angles. Secondary trabecular systems arise from the medial and lateral cortex streaming into the trochanter.

The hip joint is well protected by capsular and ligamentous reinforcements. The iliofemoral ligaments check adduction and extension; the ischiofemoral, extension, inward rotation and abduction; the pubofemoral, outward and abduction.

3.3.5.7 Functional Mobility of the Hip Joint

Movement in the hip joint is seldom carried out in one plane along; usually it is a directed movement, composite in nature, involving all three planes simultaneously. This movement is called circumpolar, in distinction from the single-plane, circumcentral movement.

3.3.5.8 Ligamentous Reinforcement of the Hip Joint

The **ligamentous apparatus** of the hip joint is very powerful, as must be expected from the wide range of motion in all planes and from the powerful dynamic effect which some motions have upon the hip joint.

The **hip joint** is amply protected by capsular as well as ligamentous reinforcements.

The **iliofemoral ligament** is divided into a superior or lateral portion which has a tensile strength of 250 kg., and an inferior or medial portion with a tensile strength of 100kg.

The ligament checks adduction especially with its upper lateral portion. All fibers tighten in extension, particularly the lower lateral portion, and its tension increases markedly toward the end of extension, at which stage it winds around the neck of the femur so that is approaches more the anterior rim of the acetabulum. Maximum tension occurs as the head of the femur, in full extension, presses forward against the ligament and the pelvis at the same time rotates backward. The iliofemoral ligament becomes tight also in extension combined with inward rotation, and in flexion combined with outward rotation.

The **ischiofemoral ligament** lies close to the lower border of the iliofemoral. It tightens in extension, in inward rotation associated with extension, in inward rotation associated with extension and in abduction.

The **pubofemoral ligament**. When the hip is in extension, this ligament checks the outward rotation. Together with the ischiofemoral ligaments, it also checks abduction. When the hip is in flexion, it checks abduction and outward rotation.

The **ligamentum teres** is an intra-articular ligament which has little mechanical function although it has considerable tensile strength, 15-57 kg., according to the book written by the german anatomist Braune, C.W. and translated later into English like "The human gait" (Braune, C.W. (1987)). It checks abduction of the femur in extension, but not before the iliofemoral ligament becomes tight. The main function of this ligament is to carry blood vessels.

3.3.6 The Hip Arthrosis (Coxarthrosis)

3.3.6.1 Anatomy of the hip and Coxarthrosis (Arthrosis of the hip)

The hip joint is composed of two bones: the femoral head and the acetabulum or socket which forms part of the pelvic bone. This joint is maintained in its place by strong ligaments and muscles and covered by a fine coating made out of cartilage that permits a wide range of motions which allow us to walk, run, jump, sit and perform all of our daily activities.

The hip joint supports all of our body weight, and because of all of our daily activities it is prone to suffer from cartilage wasting that occurs both on the femoral head and the acetabular surface (socket). This degeneration and further destruction of cartilage surface of the hip joint is known as "Arthrosis" or "coxarthrosis".

There are 2 types of coxarthrosis:

Primitive coxarthrosis occurs in a normal hip in a subject over 60 years of age and represents 40% of cases of hip osteoarthritis.

Secondary coxarthrosis occurs with hip "dysplasia" (with anatomical deformation) in a younger subject and is encountered in 60% of cases of hip osteoarthritis.

The term *degenerative joint disease* was introduced by Nichols and Richardson in 1909 [10]⁶. Nichols and Richardson described the pathological changes of osteoarthritis of the anklefoot degenerative joint disease and stressed that the degeneration of the articular cartilage was the direct cause of the disease.

This problem is accentuated by pathological conditions resulting from:

⁶Baring Garros, A. (1859), was the first to employ the designation *osteo-arthritis*, and Goldthwaite (Goldthwaite, J.E. (1940)) also applied it, as he demonstrated enlargement of the ends of bones and production of new bone near the joint. Virchow, R. (1872), preferred *arthritis deformans*. Bauer, W. and Bennett, G. A. (1937), suggested the use of the word *degenerative* as the most descriptive of the pathology of joint structure

- a. Anatomical alterations of the hip during pregnancy and birth.
- b. Congenital and hereditary factors.
- c. Work related high physical demand.
- d. Sports related high physical demand.
- e. Trauma.
- f. Old Age.
- g. Excess of weight.

The main symptom of hip Arthrosis is **PAIN**. Pain is generally felt surrounding the buttock or the groin area, but it can descend as low as the knee. At the beginning the pain is considered as being mild and can be diminished by the use of simple over-the-counter pain relievers. As cartilage degeneration and destruction advances, pain increases and limits daily activities such as walking and sitting. Thus it gets harder to control pain with over-the-counter medications.

During advanced state of the disease, pain can become constant - it is present even during rest, while lying down and during sleep. Cartilage is completely destroyed and there is direct contact between bones resulting in painful friction between surfaces. Patients may also note crackling in the hip, shortening of the limb, limping and diminished movement about the hip, with progressive limitation of daily activities. This is a common problem that affects men and women over the age of 60, but it is not infrequent to find this problem in younger patients.

3.3.6.2 Etiology and risk factors:

The joints most frequently involved in degenerative diseases are the hips, knees, intervertebral, shoulders and distal interphalangeal joints of the fingers. **Morphological abnormalities are the main risk factor for coxarthrosis**. Also

the excess of weight (overweight and obesity) and trauma and micro trauma in contact sports.

According to the Australian research mentioned before in the introduction of this document, (Retchford, T.H., Crossley, K.M., Grimaldi, A., Kemp, J.L., Cowan, S.M., 2013) the main risk factors for getting a degenerative hip disease can be plotted as follows:

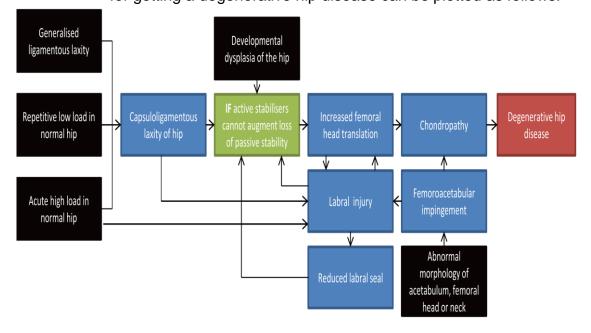


Figure 16. Proposed mechanisms for the development of degenerative hip disease as a result of multi-factorial instability. The black boxes represent the major risk factors

As we can see on the graph above the Abnormal Morphologies are considered one of the main risk factors, according to this research ours is in line with the newest findings of medicine.

The major etiological factors in degenerative joint disease are:

- a. Senescence
- b. Trauma
- c. Static deviations
- d. Constitutional predisposition.

A review of series of cases of degenerative joint disease of the hip indicates that a contributory pathological agent arose from the ilipsoatic syndrome. The syndrome is triggered into action by the erect posture in man when he has failed either to elongate the iliopsoas to a degree commensurate with his vertical growth, when the femur has rotated axially to 90, or to adapt himself to the position of Iliopsoas release by external rotation of the lower limb, mild flexion of the hips and knees, downward tilt of the pelvis and exaggeration of the lumbar lordosis attitude of the spine.

3.3.6.3 Pathomechanics of the Hip Arthrosis:

It is noteworthy that this degenerative disease is found secondarily to the previously described ilipsoatic syndromes, and the same contributing etiological factors are in part responsible.

The initial lesion is manifest not in the capsule or bone, but in the softening, erosion and degeneration of the hyaline articular cartilage; and secondly, with hypertrophic changes of the neighboring cartilage and bone attempting to bring the juxtaarticular surfaces into contact.



Figure 17.X-Rays View of Femur Bone and its insertion in Hip Joint

- a. The first changes to be noted are degeneration of the noncalcified hyaline articular cartilage and the sequence of events that is the result of softening of the cartilage, with loss of the shock absorbing action of normal articular cartilage. Gradually the softened matrix is worn down by the movements of opposing articular surfaces, until the underlying bone is exposed.
- b. In the lateral articular area a different reaction takes place; this is due to the fact that a perichondrium is present and is continuous with the synovial membrane. Here proliferative changes occur and the cartilage becomes heaped up, resulting in excrescences which have been likened to the drippings of a tallow candle. Ultimately these form osteophytes which protect the joint against movements no longer tolerated.
- c. As the cartilage is worn away the underlying bone is exposed. This gradually scleroses until it resembles ivory in consistency and appearance. This is known as eburnation. Deep to this the normal bone undergoes a process of absorption and rarefaction while at the same time new bone is laid down at the margins.
- d. In the later states changes also occur in the synovial membrane, which proliferates and becomes thickened. The fringes may undergo cartilaginous changes and become detached to form loose bodies in the joint.

- e. The synovial fluid may increase and may appear milky owing to the presence of cartilage cells.
- f. Finally, a general softening of the capsule and ligaments takes place, thus interfering with stability of the joint, with a triggered Iliopsoas predisposing to subluxation in the weight-bearing member.

Hip Arthrosis is typified by flattening the anterolateral surface of the femoral head and its corresponding acetabular support surface. Because normal contact between the femur and the acetabulum is disrupted, concentric or eccentric overload on the joint surfaces is increased; over time, this causes deterioration of local cartilaginous tissue. With the native hip, as opposed to a prosthetic hip, the joint is under significant constraint, making it more difficult to avoid the detrimental effects of contact and shear forces, which results in decreased motion, causing abutment around the hip. This is often a source for hip dysplasia, which ultimately leads to OA (Osteoarthritis). However, only recently has conclusive evidence emerged relating FAI ⁷(Femoral Acetabular Impingement) to arthritis, especially in younger patients with seemingly normal ROM ⁸(Range of movements), joint structure, and intra-articular pressure.

The origin of hip coxarthrosis has been a subject of great interest and investigation, especially within the last decade. The focus has shifted not just to treatment of the osteoarthritic hip joint,

⁷ Femoroacetabular impingement or FAI is a condition of too much friction in the hip joint. Basically, the ball (femoral head) and socket (acetabulum) rub abnormally creating damage to the hip joint. The damage can occur to the articular cartilage (smooth white surface of the ball or socket) or the labral cartilage (soft tissue bumper of the socket).

⁸ Range of Motion or ROM exercises involve moving of joints through their full pain-free range of motion. These exercises keep the joints flexible and keep stiffness at bay.

but also to the study of abnormalities in hip-fortifying structures, such as soft tissue, tendons, and periarticular bone, which may serve as precursors to degenerative changes caused by loss of joint stability and proper biomechanics. A working hypothesis explored by Ganz and co-workers (Ganz, R. et al. (2012)) has emerged to demonstrate that a number of previously classified cases of idiopathic OA (Osteoarthritis) in fact were cases of secondary OA (Osteoarthritis). caused by "minor developmental deformities" that were not appreciated with the use of conventional diagnostic and radiographic modalities⁹. Studies are beginning to show initial support to this hypothesis, most notably that these deformities play a significant role later in the development of arthritis from FAI (Femoral Acetabular Impingement). Additional studies have revealed correlations between labral lesions and acetabular retroversion and arthritis.

3.3.6.4 Evaluation:

a. Clinical findings

The symptoms observed in the presence of hypertrophic arthritis of the hip are considered as frequently the results of muscle and ligament strain. The increased forward inclination of the pelvis and the flexion of the hip, weight-thrust forces are changed and the function of the muscles about the hip is impaired. In many of these changes the action of the lliopsoas is contributory or more often causatory.

⁹[...."The etiology of osteoarthritis of the hip has long been considered secondary (eg, to congenital or developmental deformities) or primary (presuming some underlying abnormality of articular cartilage). Recent information supports a hypothesis that so-called primary osteoarthritis is also secondary to subtle developmental abnormalities and the mechanism in these cases is femoroacetabular impingement rather than excessive contact stress. The most frequent location for femoroacetabular impingement is the anterosuperior rim area and the most critical motion is internal rotation of the hip in 90° flexion"....]

Pain and muscle spasm frequently can be attributed to excessive use of the hip joint. In degenerative disease tolerance and endurance of the hip joint have diminished. If the activity is restricted to limit what the joint can accept gracefully, the symptoms often remain at a minimum. However decrease use of a joint can in itself result in further joint disintegration.

The ligamentous structures of a degenerative articulation are vulnerable to a greater degree of degeneration than are the same structures of a normal articulation. The patient appearing for examination usually is of middle age or beyond. Awkwardness of gait (psoatic) and inability to cross the leg while putting on a shoe are presenting symptoms. The onset of pathology may or may not be associated with pain. Once adaptive changes at the level of the coxofemoral joint have occurred the effects on directional mechanical movements become apparent.

The first of the movements to be restricted is internal rotation (external rotation is the first function of the Iliopsoas in the 90 axially rotated femur); and the second, extension (flexion is the second Iliopsoas function). Abduction, the third movement, is lost (adduction is the third function of Iliopsoas). Strain, fatigue and instability follow when the weight-thrust is changed and function of the muscles about the hip is impaired, with increased forward inclination of the pelvis and a stooping attitude at the hip together with externally rotated lower members.

Clinically, we have an anthropological retrogression to the status of Neanderthal Man.

b. X-Ray findings

The x-ray changes usually reflect the pathological process:

i. Degeneration and thinning of the cartilage (narrowing of joint space)

- ii. Thickening and sclerosis of the underlying bone (eburnation)
- iii. Hypertrophy of the bone at the joint margin (osteophytes)
- iv. Complete denudation of the articular cartilage (sclerosis).

Subjective symptoms and extent of degenerative findings are not always consistent with the x-ray findings. In the early stage x-ray may be entirely negative except for a convex line of sclerosis at the point of impact of the femoral head against the acetabulum. This stage may indicate a beginning softening with fibrillation of the articular cartilage.

As disuse progresses, there is degeneration with wearing away of the articular cartilage and exposure of the subchondral bone is imminent. At this time x-rays shows moderate to advanced narrowing of the coxofemoral joint space. Later, marginal proliferation is found and, clinically, impediment of joint function is noted. In the later stage, despite extensive marginal osteophytic projections synovitis is rarely present and total bony ankylosis seldom occurs.

3.3.7 Final Remarks:

As we have seen along this document the idea of the interaction of the iliopsoas muscle and the hip joint as a cause of hip diseases is not new since there are several researches that are focused on this line. But, on the other hand, there is not enough scientific evidence that can prove this intuition yet. The scope of this dissertation is to provide some scientific evidence to contribute to the development of the diagnosis and the improvement in the treatment of the hip degenerative disease to be able to cope with the huge number of patients that may develop this sickness if nothing changes in the future with particular emphasis of the iliopsoas on this degenerative

process. This is especially important as our flexion addicted sitting society moves into the above 60 ages range.

2.4. MAIN AIM:

To determine the influence of iliopsoas muscle contraction over development of hip arthrosis.

2.5. SECONDARY AIMS:

- 3.3.8 To find out the factors that determine or cause hip arthrosis
- 3.3.9 To make profiles of individuals who are likely to develop hip arthrosis in the future due to their current features of finding

2.6. HYPOTHESIS:

Demographic features of patients with Iliopsoas muscle contraction may lead to hip arthrosis and this relationship is often age and sex dependent

4 CHAPTER II. METHODOLOGY

4.1 METHODS AND TOOLS

4.1.1. DATA:

Our study was carried out in the *Muscle-Joint centre* of Netherlands during the period September 2011- September 2014. It involved 400 patients with ages in the range of 30 years old - 80 years old. All of the patients presented with hip pain and various levels of hip degeneration as seen on radiographies and/or MRI's (Magnetic Resonance Imaging). On examination all the patients had shortened iliopsoas muscle raging from 4-5 cm. This was determined by:

- 1) Relationship between left and right pelvis height in mirror , comparing with:
- 2) Leg length differences while laying face down or treatment table.

The results of this investigation can be summarized as follows according to age groups:

AGE	NUMBER	NUMBER OF	PAIN FREE	RESIDUAL
	OF	ILIOPSOAS	LEVEL	FUNCTIONALITY
	PATIENTS	TREATMENTS		

30-40	100	7	95%	Total
40-50	100	7	92%	Total
50-60	75	7	88%	Most
60-70	75	7	75 %	Most
70-80	50	7	70%	Some

Table 1. Summary of data of 400 patients presenting hip disease with stay at the Muscle-Joint centre of Netherlands

Treatment consisted of lumbar, sacroiliac and hip manipulation. Followed by passive (doctor assisted) iliopsoas elongation. Glucosamine combined with chondrotine sulphate supplements were used in 75% of the patients. Active treatment (patient done) elongation was continued at home with the primary goal of maintaining iliopsoas elongation.

A first look into these data reveals the need to be more accurate on some features, as follows:

- a) There are variables which are of quantitative nature like *age*, *number of treatments* and let us say "*Pain free level*", since although this last variable is more qualitative than quantitative it has been transformed into a quantitative one.
- b) The number of elements of the sample is n = 400, that is, the number of persons affected by *hip disease in this study*. This number can be considered big enough according to the *large numbers law* that give mathematical support to the *central limit theorem¹⁰*, in reality scientists usually consider that 30

¹⁰ The central limit theorem, although we could speak in reality of central limit *theorems*, since there are several authors that reached different conclusions, consists in the application of mathematical convergence of number series to reach normality conditions for random variables,

elements are a large enough sample as to guarantee **normality** conditions. Although the number of elements to be sampled from population (In our case the overall number of people **sick** with hip disease) depends on the purpose and the methodology of the research.

- c) In reality the nature of our data is pretty suitable for multivariate methods, which are the common statistics tools used for this kind of problems, since the factors that explain the phenomenon are of a quantitative nature and, at the same time, the variables that measure the impact in the dependent variable, let us say, the severity of the hip disease are of qualitative nature. That is the case of the variable named *Functionality* altogether with the abovementioned *Pain free level* variable which, both of them put together, remind me a lot of the ASIA scale used for measuring the severity of spinal cord injury¹¹. We could apply a similar scale consisting in five degrees of severity ordered, for instance, from more pain and less functionality (A) to less pain and more functionality (E).
- d) According to the nature of data as explained above we could apply multivariate methods, specifically *Classification Methods*. The most interesting statistical methods for the current research being:

as we have in our experiment. For further details about this theory please read Ruíz-Maya Pérez, L. & Martín-Pliego López, F.J. (2008).

¹¹ The ASIA Impairment Scale assigns five degrees of severity to those people with spinal cord injury, as follows: A = Complete; B = Sensory Incomplete; C = Motor Incomplete; D = Motor Incomplete; E = Normal. For further details please read Van Den Berg, M., Castellote, J.M, Mahillo-Fernandez, I. (2012)

4.1.2 METHODS:

4.1.2.1 Discriminant Factorial Analysis:

This technique consists in reducing the scale of the problem. Suppose we have a big number of factors that influence the dependent variable, in our investigation this variable would be called "*Degree of Severity of Hip Disease*", we can join these explaining variables or factors into a few factors which would be called by different names and summarize the original information. In the end we can set some boundaries for every region of the

dependent variable, that is, in our study case, and assuming that we follow a scale somehow similar to **ASIA Impairment Scale**, we would have three regions of severity, namely "A", "B" and, "C". If we layout our data on a two axes graph we would have, following to Peña, D. (2002) a drawing of this kind:

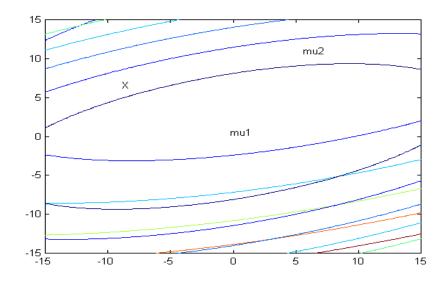


Figure 17. Equidistant Curves according to Mahalanobis Index. Source: Peña,D. (2002)

Being this drawing a kind of weather map in which every curve has got a different colour indicating a different level of the variable, in our example there would be three curves, namely "A", "B" and "C".

May be this example seems a little bit tough for an introduction to the subject. Let us show an example of a basic model consisting of just two explaining variables and one dependent variable, then the final graph obtained through the application of the Discriminant Factorial Analysis algorithm would give us a Discriminant Function in dotted lines as follows:

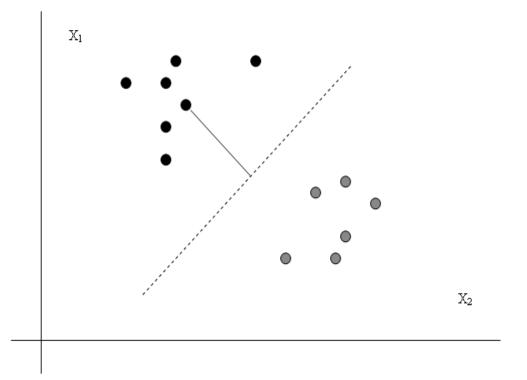


Figure 18. Discriminant Function as a boundary for the two possible groups of the dependent variable

In this example, very simple but very intuitive, we can see that the dotted line representing the Discriminant Function in reality is a boundary that splits the observations into two groups. Let us imagine that we have a group of patients with different features then this line could set the boundary between the group of survivors to a very deadly sickness and the group of nonsurvivors to such a sickness. We can have a lot of information of all kinds, both quantitative and binary variables, from the sample of patients, but the algorithm of the Discriminant Factorial Analysis will summarize all of this information in only a few factors, in the graph above there are only two final factors, x_1 and x_2 , which levels in the sample will determine to be in one side or another of the dotted line, in the example of the deadly sickness would mean to be on the side of the survivors or on the side of the dead people.

But as we have said in the beginning of this section we need a lot of variables and according to the Table 1 we have just a few of factors like **age, gender** and **number of Iliopsoas Treatments**. The answer is that in reality the number of factors that influence the **degree of severity of hip disease** is much bigger. Let us just recall what we suggested in section 1.6.1 about risk factors for getting sick with hip arthrosis:

- a. Anatomical alterations of the hip during pregnancy and birth.
- b. Congenital and hereditary factors.
- c. Work related to high physical demand.
- d. Sports related to high physical demand.
- e. Trauma.
- f. Old Age.
- g. Excess of weight.

But in reality we can split some factors in several more since, for instance, **Sports related to high physical demand** can be split into new factors like, for instance, **number of hours of** *sport* x_i and this for every sport. The same can be done for the factor *Work related to high physical demand*. And so on.

4.1.2.2 Regression Models:

A Multivariate Linear Regression:

This technique minimizes the *square distance* between the cloud of data and the regression function proposed by the model and obtains in this way the value of each coefficient of the explaining variables. Just to have an idea of the technique we can show it by adding a layout as follows:

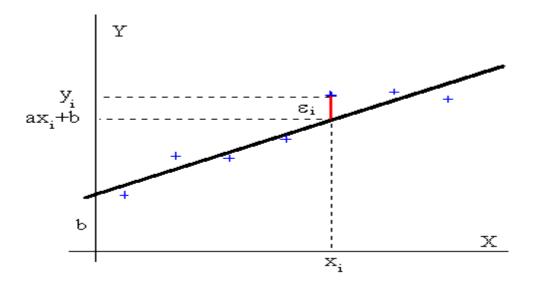


Figure 19. Graphic description of the Ordinary Least Squares Regression Method

Therefore we will have to minimize the length of all red coloured bars of our model, but this will be performed by a personal computer through the Statistical Program for Social Sciences, widely spreaded around the scientific community, and popularly known as **SPSS.**

An additional matter arises from the need of this kind of models to fulfill a set of assumptions that in case of not being true may make null all the conclusions obtained through the application of the technique.

The *assumptions* to be fulfilled are those of any General Regression Model that use the technique of *Ordinary Least Squares*, for the linear case, since after the logarithmic transformation is what we have, a simple *Multivariate Linear Regression Model*, being these assumptions the following ones:

i. Linearity:

As an average the explaining variables have a linear relationship with the dependent variable, that is, the Regression Function set by the technique of Ordinary Least Squares goes through the averages of both dependent and independent variables. This means that:

$$\bar{y} = \hat{a} + \hat{b} * \bar{x} \quad (1)$$

This also means that the positive and the negative deviations for the random term ε_i are zero as an average. That means:

$$E(\varepsilon_i) = 0 \forall i$$
 (2)

ii. Independence:

Random terms between items of the sample are stochastically independent, patient in our research, that means:

$E(\varepsilon_i\varepsilon_j) = 0 \ \forall \ i \ \neq j \quad (3)$

This means that the severity of hip arthrosis for patient *i* does not depend on the severity of hip arthrosis observed in patient *j*, since the only randomness of the model is due to the randomness of random terms ε_i .

iii. Homoscedasticity:

The variance of random terms ε_i keeps constant for every sample item and does not depend on the values taken by the explaining variables. This means that in our case there is homogeneity among patients. Mathematically:

 $Var(\varepsilon_i) = \sigma^2 \forall i \qquad (\mathbf{4})$

iv. Normality:

The random terms of the Linear Regression Model, ϵ_i , behave in probability like a Normal Distribution, that way putting all assumptions together we would get:

 $\varepsilon_i i.i.d \sim N(0,\sigma^2) \forall i$ (5)

This means that random terms for every patient behave like independent variables that follow a Normal Probability Distribution with average 0 and Variance σ^2 .

As the dependent variable of this kind of models is just the addition of a deterministic part, as seen in (1), and a random term ε_i , it means that:

 $y_i = \hat{a} + \hat{b} * x_i + \varepsilon_i \ i.i.d \sim N(\mu_y, \sigma^2) \ \forall i$ (6)

Being μ_y the average or expected value of the observations of the dependent variable.

These four assumptions can be shown altogether on a graph according to Justel, A. (2005):

Figure 20. General Assumptions of Linear Regression Models using Ordinary Least Squares Technique

Linearity since the observations can be displayed around a straight line, *Normality* given that the observations can be included under the bell curve, Gaussian curve, defined by the normal probability distribution, *Homoscedasticity* since the range of possible values taken by the observations of the dependent

variable is always the same it does not matter what value is taken by the independent variable, or explaining variable, of the model.

v. Multicolinearity:

Multicolinearity appears in the model when the explaining variables correlate among them. Then it is pretty hard to split their effects and to measure the individual contribution of every explaining variable to the value taken by the dependent variable, giving this way to instability in the estimates of the coefficients assigned to the explaining variables which will also have a big variance.

vi. Autocorrelation:

Autocorrelation can be defined as the correlation among random terms along time. The main consequences of this are:

- a. Estimates of explaining variables coefficients are unbiased but not efficient
- b. Assumption Tests for such coefficients are not valid.
- c. Forecasts are not reliable at all.

In case of autocorrelation is advisable to use *Time Series Models* instead of *Regression Models*.

B Logistic Regression:

A second Statistics Technique for Regression Models that could be used is called "*Logistic Regression*", that consists in a specific kind of *Multivariate Regression Model* in which the dependent variable is a categorical one, like in our research that we have three possible values for the dependent variable *degree of severity of hip disease*.

But since the dependent variable proposed by the Logistic Regression Model is a probability, in our case there would be three categories for the dependent variable, *degree of severity of hip disease*, and therefore there would be three probabilities, every of them assigned to one category of severity between A and C, the values of the dependent variable need to be hedged between 0 and 1 to fulfil the properties of probability axiomatic and the best way to get this is by using a S-shaped curve, by the way a little bit like a human backbone, called logistic curve, as it can be seen below:

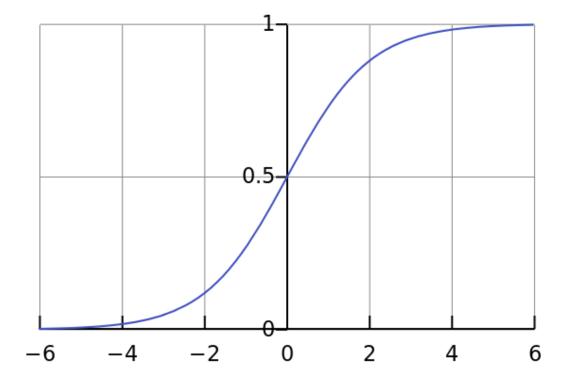


Figure 21. Logistic Curve used for Logistic Regression

Therefore we need to adjust our cloud of data to this new curve instead of adjusting it to the straight line that we showed before.

$$p_i = \frac{1}{1 + e^{-(\alpha + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k)}}$$
(7)

But for mathematical easiness we will transform the model with double logarithms in both sides of the original equation giving us the following final formula:

$$Log (OR) = Logit(pi) = \log_e(pi/(1-pi)) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k$$
(8)

Being OR the Odd ratio between the probability of happening A and the probability of happening B, in our research A and B would be two different degrees of **severity**, our dependent variable.

As it can be seen this equation only allows to include two categories, due to the intrinsic definition of Odd Ratio, what would mean that we should add more equations for including the rest of the categories of our dependent variable.

Just to show an example we can follow García Pérez, E. (García Pérez, E. ; Manchado, B., 2008):

$$log \frac{P_{i}(l)}{P_{i}(0)} = \mathcal{S}_{10} + \sum_{h=1}^{H} \mathcal{S}_{1h} \cdot X_{hi}$$
$$log \frac{P_{i}(2)}{P_{i}(0)} = \mathcal{S}_{20} + \sum_{h=1}^{H} \mathcal{S}_{2h} \cdot X_{hi}$$
$$log \frac{P_{i}(3)}{P_{i}(0)} = \mathcal{S}_{30} + \sum_{h=1}^{H} \mathcal{S}_{3h} \cdot X_{hi}$$

In this example we are dealing with a model of Logistic Regression for a categorical variable of four categories, the base category is assigned a "0" and the other three categories are assigned the values "1", "2" and "3" respectively.

In our case we will have to remove one equation, since we have three categorical values for our dependent variable *degree of severity of hip disease*, that is equivalent to say that we have to solve two binary logistic regression models and the calculations are not easy being necessary iteration methods of the Newton-Raphson kind¹², but these calculations can be performed efficiently a one more time by our PC through *SPSS*.

The calculations performed through the Newton-Raphson algorithm will allow us to work out the estimates of the coefficients of the independent variables. The complexity of this algorithm arises from the mathematical expression used by the "Maximum Likelihood Method" instead of the "Ordinary Least Squares" Method used by General Linear Multivariate Regression.

The first step is to work out this "**Likelihood Function**", that is, the likelihood of getting the sample that we have, conditioned to the parameters that we want to estimate, in our case the coefficients of the explaining or independent variables.

¹² For further development of this algorithm please read Peña, D. (2002)

Mathematically it can be explained like this:

$$L(\underline{\overline{X}}/\overline{\theta}) = \prod_{i=1}^{n} f(x_i, \overline{\theta})$$
(9)

Being

 $L(\overline{X}/\overline{\theta})$ Likelihood Function of the sample conditioned to a θ parameters vector

 $f(x_i, \overline{\theta})$ probability density function of x_i sample element, with θ parameters vector

Second, after calculating this Likelihood Function, the vector of parameters, $\overline{\theta}$, can be worked out through an equations system resulting from the first derivatives of the likelihood function with respect to the $\overline{\theta}$ vector of parameters.

$$\frac{\partial L(\overline{X}/\overline{\theta})}{\partial \theta_1} = 0$$

$$\frac{\partial L(\overline{X}/\overline{\theta})}{\partial \theta_2} = 0$$
.....
(10)
....
$$\frac{\partial L(\overline{X}/\overline{\theta})}{\partial \theta_k} = 0$$

Taking into account that the expressions for the probability density functions can be more or less complex, like in equation (8), this explains the need for very powerful algorithms, like Newton-Raphson, which will be included among the annexes to this document.

4.1.2.3 Clusters Analysis:

This technique is not a Classification Technique but rather a Descriptive Technique, although very useful since it allows to create profiles from sample information. We could, in our research, to create profiles of patients according to the different categories of the dependent variable, degree of **severity of hip arthrosis**, this way we could get a **robot portrait** of the kind of patients to be assigned to every degree of severity from A to C.

We will show a common Cluster Dendrogram; this kind of graph was introduced in Science by Linneo for Species Classification purposes:

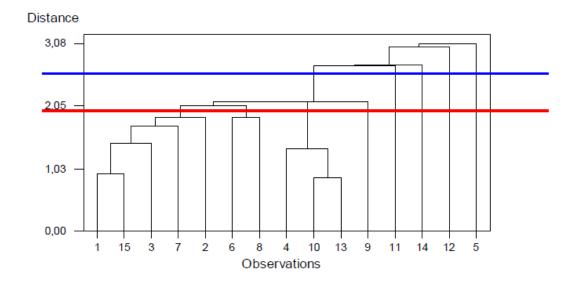


Figure 22. Dendrogram graph for Cluster Analysis. Source: Universidad Oberta de Catalunya.

The Y axis represents here the distance to the centroid of the cluster from a given cluster element , this distance may be calculated as a very simple distance like The *Euclidean Distance,* which is a direct application of Pythagoras Theorem to Cluster Analysis, or a more sophisticated one, like Mahalanobis Distance, which takes into account the variances of the clusters¹³.

Every of the clusters shown above, the rectangular areas numbered from 1 to 15, can give us a profile of patient corresponding to every category of **severity** that could be applied in our research.

4.1.2.4 Analysis of Variance (ANOVA):

This technique is neither a Classification Technique nor a Descriptive one, it is rather a technique for "**Factorial Analysis**", like "**General Regression Techniques**" and "**Discriminant Factorial Analysis**", that will allow us to set if a factor, like sex, age, daily activity, etc., influences the dependent variable, in our case, "severity", in some degree to be defined by the researcher through the "**Significance Level**". This significance level is usually named by the letter " α " and means the probability of rejecting the "Null Hypothesis" of the experiment when it is true in reality; this is why it is called the probability of making a "**Type I Error**"¹⁴.

The conditions to be able to use this technique are:

¹³ For further learning about this matter please read Peña,D. (2002)

¹⁴ As it can be found in Casas, J.M.(1997)

- a. The dependent variable must be quantitative.
- b. The Independent variables are "Factors" and therefore must be categorical, qualitative, variables.
- c. The assumptions through which this technique is efficient are the same that those that we have already described in "Logistic Regression" as "basic" assumptions for General Regression Models (Linearity, Independence, Normality, Homoscedasticity) without minding the other two assumptions called "Autocorrelation" and "Multicolinearity".

The assumptions are the same that we use in Regression since this technique is somehow the other side of the coin with respect to that technique. In fact the final statistic to test the influence of factors over the dependent variable is also used in Regression Models through Pearson's Linear Determination Coefficient, which has got the following mathematical expression:

$$R^{2}_{x,y} = \frac{S_{Y}^{2}}{S_{Y}^{2}} = (R_{x,y})^{2}$$
(11)

Being:

 $R^{2}_{x,y}$ Pearson's Linear Determination Coefficient between x and y

 S_{Y}^{2} Predicted Values Variance obtained by Regression Model through Ordinary Least Squares

 S_{Y}^{2} Observed Values Variance for dependent variable

In reality the technique of ANOVA just compares the "Variance within-groups" to the "Variance among-groups" and uses this ratio as the "**F statistic**" to test the "**Null Hypothesis**", taking into account that the probabilistic behaviour of the above mentioned statistic is that of a "**Fischer-Snedecor Distribution**", also called "F Distribution", and for which a range of values have got defined probabilities that can be retrieved from a Probability Table.

From a mathematical point of view all the above can be expressed like this:

	source	sum of squares	degrees of freedom	mean square	EMS	variance ratio
_	F	SS(F)	$n_F - 1$	$\frac{\mathrm{SS}(F)}{n_F - 1}$	$\frac{\left\ \boldsymbol{\tau}_{F}\right\ ^{2}}{n_{F}-1}+\sigma^{2}$	$\frac{\mathrm{MS}(F)}{\mathrm{MS}(\mathrm{residual})}$
	G	SS(G)	$n_G - 1$	$\frac{\mathrm{SS}(G)}{n_G-1}$	$\frac{\left\ \boldsymbol{\tau}_{G}\right\ ^{2}}{n_{G}-1} + \sigma^{2}$	$\frac{\mathrm{MS}(G)}{\mathrm{MS}(\mathrm{residual})}$
	F-by-G	$\mathrm{SS}(F\wedge G)$	d_{FG}	$\frac{\mathrm{SS}(F\wedge G)}{d_{FG}}$	$\frac{\left\ \tau_{FG}\right\ ^2}{d_{FG}} + \sigma^2$	$\frac{\mathrm{MS}(F \wedge G)}{\mathrm{MS}(\mathrm{residual})}$

Figure 23. ANOVA Table. Source: Bailey, R.A. (2008)

The first column above specifies the source of variation for Data, in this case there are two factors F and G.

The second column works out the sum of squares of deviations between every element and the average, that is, the "Numerator" of the Variance expression.

The third column indicates the number of "Degrees of Freedom", that is, the number of variables less the number of estimates performed for the parameters of the model. The fourth column is the "Mean Square" and it is the expression of the "Variance", obtained by the division of second and third column (Sum of Squares of every variation source split by the Degrees of Freedom).

The sixth column performs the calculation of the ratio above mentioned to compare Within-groups Variance to Between-groups Variance. That is the expression of the statistic to be used for Hypothesis Testing purposes.

Finally most of statistical programs, like SPSS, give a last column with the p-values, that allows the researcher to perform "Decision Making".

4.1.3 DATA REVIEW:

There are three different techniques that we can use to classify our data, namely *Discriminant Factorial Analysis* and *Logistic Regression*.

Every of these techniques will usually provide us the same results, that is, the same Classification Matrix. This way we can *check* our results just with one statistical program, SPSS, without needs of an additional tool.

There is an extra technique called *Cluster Analysis* that seems to be very useful for creating *profiles* of patients according to every category of the variable *severity*.

Finally the "**Analysis of Variance**" technique provides us with a powerful tool for Experiments Designs purposes which will set the influence of every factor over the dependent variable.

The statistical programs that will be used for all calculations purposes will be **SPSS** and **Excel**.

Regarding the data to be used in calculations and according to point 1.6.1 and the abovementioned related to *Discriminant Factorial Analysis*, it would be advisable to get more data from patients.

The "optimal" data set to work with *could* include the following fields:

- i. Date of Birth.
- ii. Gender.
- iii. Weight.
- iv. Height.
- Trauma: Boolean variable that will have the value "Y" in case of traumatic accident involving the iliopsoas area and "N" otherwise.
- vi. Congenital Factors: Inheritance about hip arthrosis in the family.
- vii. Number of hours per week of physical work.
- viii. Number of Passive Treatments by Doctors.
 - *ix.* Number of hours per week of gymnastics at Home for Reinstatement.
 - *x.* **Degree of Hip Arthrosis** (values from A-C as mentioned before).
 - xi. Sport 1 (Category, for instance: Soccer)
- xii. Number of hours per week of sport 1
- xiii. Sport 2 (Category, for instance: Tennis)
- xiv. Number of hours per week of sport 2

And so on for all sports.....

4.1.4 FINAL DATA:

The final Data Base (DB) has not too many of the factors included in section 3.1.3, and it includes only five fields, as follows:

- a. Age
- b. Gender
- c. Kind of Arthrosis
- d. Number of Treatments
- e. Percentage of Functionality Restored (This variable is called Results in the DB)

These data are very good for performing ANOVA as it includes four factors and the dependent variable is a quantitative one. These data are also good for multivariate methods like the Classification techniques described above since although the dependent variable is quantitative it can be easily categorized according to the ASIA kind of scale proposed on section 3.1.1 of this document.

4.2 ANALYSIS AND RESULTS:

The analysis will be performed for the "**Evolution of Arthrosis**" due to the kind of data that we have, that means that all factors, "Gender", "Age", "Number of Treatments" and "Kind of Arthrosis" will be analyzed to determine their influence over the "Evolution of Arthrosis" variable, measured by the "Pain Free Level", which consists of a percentage, being this last variable of a quantitative nature.

Therefore, we will use the "Evolution of Arthrosis" variable in both quantitative and qualitative, categorical, forms. Which one will be used on the analysis will depend on the kind of analysis to be performed. For instance, Analysis of Variance needs to use the quantitative version while the Classification Techniques, Logistic Multivariate Regression and Discriminant Factorial Analysis will use the qualitative one.

This is not the only case in which we will need to keep a double version of a variable, since the same happens with "Number of Treatments". This variable will be taken as categorical or qualitative for Analysis of Variance technique while it will be taken as quantitative for the rest of them.

The conversions to qualitative from quantitative will be performed considering the Table 1 above on section 3.1.1 which will experience some changes as follows:

NUMBER	NUMBER	
OF	OF	
ILIOPSOAS	ILIOPSOAS	
TREATMEN	TREATMEN	
TS	TS	
quantitativ	categorical	
е		
7-9	А	
10-12	В	
13-15	С	

Table 2. Transformation of "Number of Treatments" from quantitative to categorical

PAIN FREE LEVEL quantitativ e	RESIDUAL FUNCTION ALITY	PAIN FREE LEVEL categorical
100%-89%	Total	А
88%-71%	Most	В
70 %-0%	Some	С

Table 3. Transformation of "Pain Free Level" from quantitative to categorical

- "Number of Iliopsoas Treatments categorical" variable will be described in three categories¹⁵ of the same range width ordered from A to C, corresponding A to the lowest values and C to the highest ones.
- "Pain Free Level categorical" variable will be described in three categories with different range width ordered from A to C, corresponding A to the highest values and C to the lowest ones, taking into account as classification criterium the "Average of Functionality" recovered by patients according to the study carried out in The Muscle-Joint Center of Netherlands.

3.3.10 Sample Descriptive Statistics Analysis:

¹⁵ Note that according to our Data Base all patients are registered with the same number of treatments, 7, and in this case the "Number of Iliopsoas Treatments" variable cannot be considered a variable anymore and it will be just considered as one more assumption of the research.

> By Age:

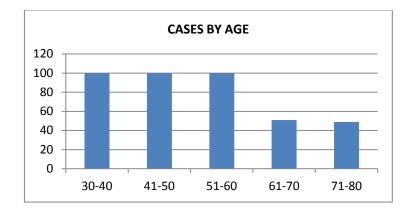


Figure 24. Number of cases by Age obtained by Excel. Source: Own Design through The Muscle-Joint Center of Netherlands data

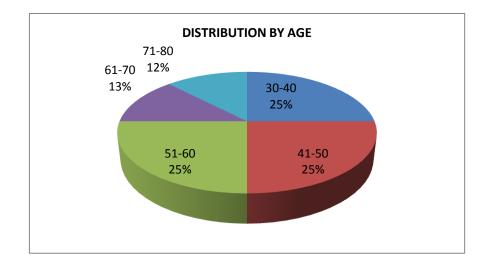


Figure 25. Distribution of sample by age obtained by Excel. Source: Own Design through The Muscle-Joint Centre of Netherlands data

We have a sample of 400 patients above 29 years old, well balanced in the first three categories of age counting for a quarter

of the sample per each, and in the last two categories of age, patients count for the remaining quarter of the sample.

The average age is 51, 56 years old, being this figure a good indicator of the variable since the standard deviation is much smaller, 13,837 years old, meaning that the sample is very homogenous¹⁶ with respect to age.

F		
Ν	Valid	400
	Missing	0
Mean		51,56
Median	I	50,50
Mode		43 ^a
Std. De	eviation	13,837
Skewne	ess	,364
Std. Er	,122	
Kurtosi	-,805	
Std. Er	,243	
Minimu	30	
Maximu	80	
Percen	tile 25	40,25
S	50	50,50
	75	60,75

Statistics

AGE

a. Multiple modes exist. The smallest value is shown

Figure 26. Main Descriptive Statistics obtained by SPSS. Source: Own Design through The Muscle-Joint Centre of Netherlands data.

> By Gender:

¹⁶ The Homogeinity of data is usually measured by Pearson's Variance Coefficient which aceptable values are between 0 and 1, being its expression the Standard Deviation split by the Mean. For further deepening in this feature please read Amón, J. (2006).

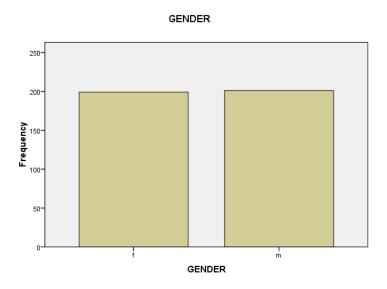


Figure 27. Number of cases by Gender obtained by SPSS. Source: Own Design through The Muscle-Joint Centre of Netherlands data

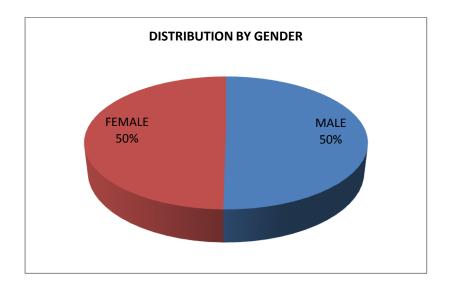
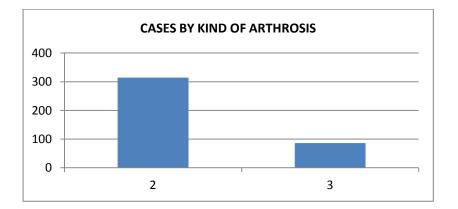


Figure 28. Distribution of Sample by Gender obtained by Excel. Source: Own Design through The Muscle-Joint Centre of Netherlands data

As it can be seen from both graphics the design of the study has been carefully planned counting for both men and women in the same proportion. This way there will be no "**bias**" by gender in the selection of the sample. There are just two more men than women in reality, as it can be seen in the table below:

	GENDER	FREQUENCY
MALE	m	201
FEMALE	f	199

Table 4. Number of patients sampled by Gender obtained by Excel.Source: Own Design through The Muscle-Joint Centre of Netherlandsdata



> By Kind of Arthrosis:

Figure 29. Number of cases by Kind of Arthrosis obtained by Excel. Source: Own Design through The Muscle-Joint Centre of Netherlands data.

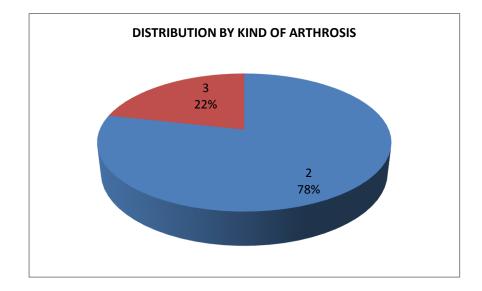


Figure 30. Distribution of Sample by Gender obtained by Excel. Source: Own Design through The Muscle-Joint Centre of Netherlands data

As it can be seen in this case the sample is biased by Kind of Arthrosis since the number of cases of Arthrosis Type 2 is much bigger than those of Arthrosis Type 3. The consequences of this bias for this variable, Factor, will have to be determined carefully.

> By Evolution of Arthrosis:

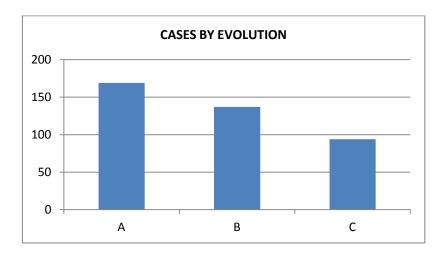


Figure 31. Number of cases by Evolution of Arthrosis obtained by Excel. Source: Own Design through The Muscle-Joint Centre of Netherlands data.

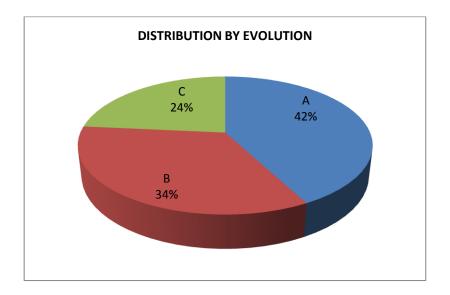


Figure 32. Distribution of Sample by Evolution of Arthrosis obtained by Excel. Source: Own Design through The Muscle-Joint Centre of Netherlands data

Here we cannot speak of "bias" because in fact this is just a "Result" after analyzing the sample. It would be interesting to analyze the quantitative version of this variable too since this is the dependent variable and, for some techniques that we are going to apply, "**Normality**" of data for dependent variable is needed.



Figure 33. Histogram of frequencies of Evolution of Arthrosis obtained by SPSS and comparison to Normal Probability Distribution curve. Source: Own Design through The Muscle-Joint Centre of Netherlands data

It seems clear according to the graph above that there is No-Normality of data with respect to the Evolution of Arthrosis variable, although this has to be analyzed more deeply after getting some results.

3.3.11 Clusters Analysis:

We have performed a two-step cluster analysis since it is the most complete allowing including both quantitative and categorical variables. This kind of Cluster Analysis in two steps is a combination of "k-Means Cluster Analysis" and "Hierarchical Cluster Analysis". The results obtained by SPSS are as follows:

3.3.11.1 Results:

Model Summary



Cluster Quality

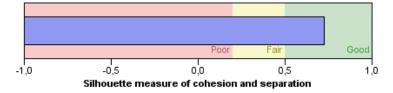


Figure 34. Quality of Cluster Analysis as performed by SPSS. Source: Own Design through The Muscle-Joint Centre of Netherlands data

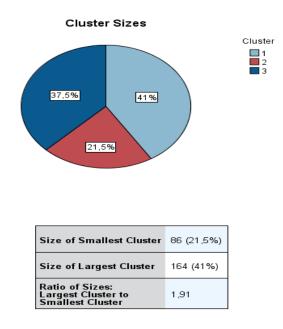
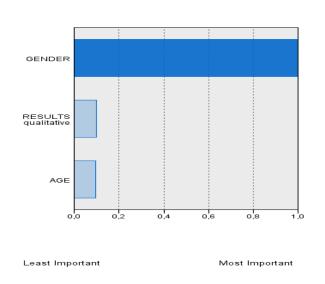


Figure 35. Size of Clusters as performed by SPSS. Source: Own Design through The Muscle-Joint Centre of Netherlands data



Predictor Importance

Figure 36. Importance of Factors as predictors of the Clusters as performed by SPSS. Source: Own Design through The Muscle-Joint Centre of Netherlands data

Clusters

Input (Predictor) Importance

Cluster	1	3	2
Label			
Description			
Size	41,0% (164)	37,5% (150)	21,5%
Inputs	GENDER	GENDER	GENDER
	1,00	0,00	0,43
	AGE	AGE	AGE
	48,74	49,02	61,37
	ARTHROSIS KIND	ARTHROSIS KIND	ARTHROSIS KIND
	1,00	1,00	0,00
Evaluation Fields	RESULTS qualitative	RESULTS qualitative	RESULTS qualitative
	A (50,6%)	A (47,3%)	C (55,8%)

Figure 37. Size of Clusters as performed by SPSS. Source: Own Design through The Muscle-Joint Centre of Netherlands data

According to these results we can have a preliminary idea of what factors influence evolution of arthrosis and in what sense.

The most important factor for clustering is "Gender" at a level of almost a 100%, the rest of factors are not very important as their correlation coefficients are less than 0, 2 as it can be seen on Figure 36.

Figure 37 is the most useful output generated by SPSS since it allows us to create profiles for every cluster. In this line Clusters 1 and 3 include patients of about 49 years old, with patients of Cluster 1 being men and patients of Cluster 3 being women. Both Clusters contain mainly patients with Type III Arthrosis and are mainly related to Evolution of Arthrosis class A,

which means that patients that belong to this cluster are those with the best evolution after treatment. But these results in reality do not mean too much due to the fact that Gender, being the most important factor to determine the Cluster, is different for both Cluster 1 and 3 and the rest of Factors are not statistically significant.

The other Cluster, Cluster number two, is made basically of people about 61 years old with Type II Arthrosis and in it men and women are fifty-fifty, since gender is the only clear factor to determine the Evolution of Arthrosis not too many conclusions can be obtained from this cluster too.

3.3.12 Analysis of Variance (ANOVA):

3.3.12.1 Model Specification:

Since we have three factors, Gender, Age and Kind of Arthrosis, and all of them may generate interactions that influence the dependent variable we will consider a "3 way ANOVA with Interactions Model" which can be expressed like this:

 $Y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_k + \alpha\beta_{ij} + \alpha\gamma_{ik} + \beta\gamma_{jk} + \alpha\beta\gamma_{ijk} + u_{ijk}$ (12)

Being:

 Y_{ijk} Observed values of dependent variable with respect to item i from factor α , item j with respect to factor β and item k with respect to factor γ

 μ Overall average of the sample

 α_i Effect from factor α for item i

 β_i Effect from factor β for item j

 γ_k Effect from factor γ for item k

 $\alpha\beta_{ij}$ Joint Effect from interaction of α and β factors for items i and j respectively

 $\alpha \gamma_{ik}$ Joint Effect from interaction of α and γ factors for items i and k respectively

 $\beta \gamma_{jk}$ Joint Effect from interaction of β and γ factors for items j and k respectively

 $\alpha\beta\gamma_{ijk}$ Joint Effect from interaction of α , β and γ factors for items i, j, and k respectively

 u_{ijk} Error Term for item i from factor α , item j from factor β and item k from factor γ

Replacing these theoretical variables for the real ones used in our model:

 $Evolution_{ijk} = \mu + Age_i + Gender_j + ArthrosisKind_k + Age * Gender_{ij} + Age * ArthrosisKind_{ik} + Gender * ArthrosisKind_{jk} + Age * Gender * ArthrosisKind_{ijk} + u_{ijk}$ (13)

3.3.12.2 Results:

Estimated Marginal Means of RESULTS

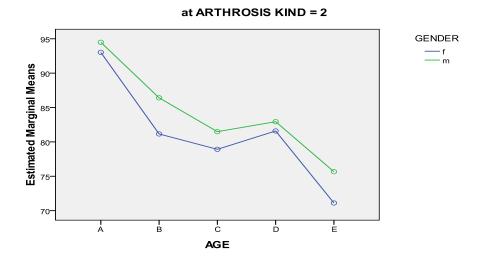


Figure 38. Marginal Means Plot for Type II Arthrosis as obtained by SPSS

Estimated Marginal Means of RESULTS

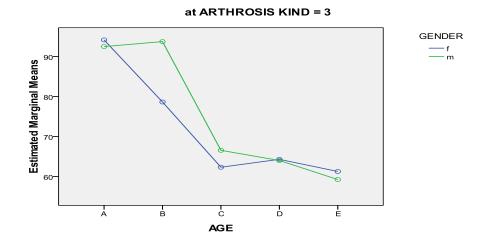


Figure 39. Marginal Means Plot for Type III Arthrosis as obtained by SPSS

As it is shown on previous figures "**Gender**" seems to be an influencing factor for the marginal means of Evolution, that is, for the means of every sub-group of data according to Age, (split by category according to five levels, A to E, corresponding A to the lowest values and E to the highest ones), and "**Arthrosis Kind**" as well since Type III Arthrosis has a much greater slope, negative slope, on both male and female "Pain Free Levels", measurement of the "Evolution of Arthrosis" dependent variable.

Detailed results of the Analysis can be found on the table below with validation tests for them:

Dependent Variable:RESULTS									
Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared			
Corrected Model	41421,890ª	19	2180,099	12,072	,000	,376			
Intercept	1168629,431	1	1168629,431	6470,953	,000	,945			
AGE	15569,561	4	3892,390	21,553	,000	,185			
GENDER	446,836	1	446,836	2,474	,117	,006			
ARTHROSISKIND	3883,623	1	3883,623	21,504	,000	,054			
AGE * GENDER	670,768	4	167,692	,929	,447	,010			
AGE * ARTHROSISKIND	3425,543	4	856,386	4,742	,001	,048			
GENDER * ARTHROSISKIND	,014	1	,014	,000	,993	,000			
AGE * GENDER * ARTHROSISKIND	408,634	4	102,159	,566	,688	,006			
Error	68626,547	380	180,596						
Total	2771025,000	400							
Corrected Total	110048,437	399							

Tests of Between-Subjects Effects

a. R Squared = ,376 (Adjusted R Squared = ,345)

Figure 40. ANOVA Table as obtained by SPSS

As it can be seen on Figure above, the ANOVA Table gives p-values very close to zero for all Factors except for those related to "Gender", which have been marked in red. This means that the Hypothesis for every factor being irrelevant, that is, that the average is the same in all subgroups of the factor, would be rejected, in case that all assumptions of the model were true, with a very small mistake probability, actually the "**significance level**" has been set to 0,05 (5%), for all factors but "Gender" and its interactions. That would mean in a priori analysis that:

- I. $H_0: \alpha_i = 0$ is not true. Age is relevant
- II. $H_0: \beta_i = 0$ is true. Gender is not relevant
- III. $H_0: \gamma_k = 0$ is not true. Kind of Arthrosis is relevant
- IV. $H_0: \alpha \beta_{ij} = 0$ is true. Age-Gender Interaction is not relevant
- V. $H_0: \alpha \gamma_{ik} = 0$ is not true. Age-ArthrosisKind Interaction is relevant
- VI. $H_0: \beta \gamma_{jk} = 0$ is true. Gender-ArthrosisKind Interaction is not relevant
- VII. $H_0: \alpha \beta \gamma_{ijk} = 0$ is true. Age-Gender-Arthrosis Kind Interaction is not relevant

These results, mainly that "**Gender**" and all its interactions with the other factors of the model would not be an influence factor, are in line with the results obtained through Cluster Analysis, but we have to check that the basic assumptions of the model are true.

3.3.12.3 Assumptions Validation:

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The assumptions to be fulfilled are the same to those of the General Regression Model which have been deeply explained on section 3.1.2.2. of this document, "Multivariate Logistic Regression":

- > Linearity
- Independence
- Homoscedasticity
- Normality

The difference with respect to General Regression Models is that in Analysis of Variance Technique the effect of not fulfilling some basic assumptions, like those of Normality or Homoscedasticity is not as big as it was on Regression Models. Following Martínez-González, Miguel A. et al., (2009) they say that only in case of small samples, less than 30 items per sub-group, and strong nonfulfilments of the basic assumptions of the model, ANOVA model should be replaced by others like Kruskal-Wallis Test.

In our sample, in spite of having a big sample of 400 patients, due to be analyzing by three factors at the same time, there can be small groups, in fact we have a subgroup that includes only 7 people (For "D" and "E" Age Group, and Arthrosis Kind equal to "3", both men and women make small sub-groups). Even joining Age Groups "D" and "E", that is, men and women over 61 years old, there would be small sample sizes for all subgroups with Arthrosis Kind equal to "3", therefore it seems to be a must to check the fulfilment of the above mentioned assumptions.

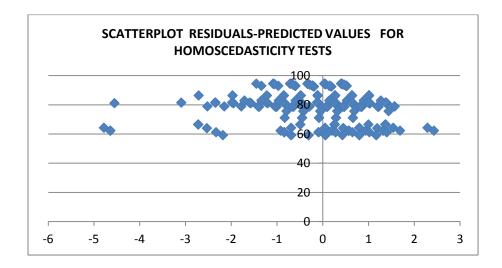


Figure 41. SCATTERPLOT between Standardized Residuals and Predicted Values for "Evolution" generated by ANOVA Model through SPSS

It seems from graph above that Homoscedasticity of residuals is fulfilled since the variance of Standardized Residuals, on X axis, for every predicted value of dependent variable, on Y axis, is more or less constant.

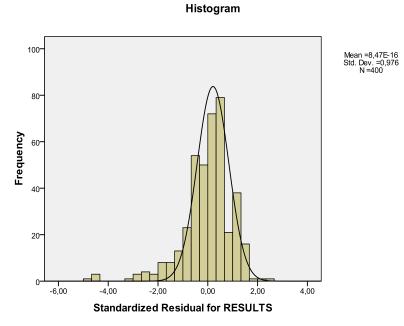


Figure 42. Standardized Residuals Frequencies Histogram and Normal Probability Curve generated by ANOVA Model through SPSS

It seems hard to set the fulfilment of Normality Assumption for Standardized residuals only from Figure above so additional tests are needed.

Informe de StatTools	
Análisis:	Prueba de normalidad Chi-cuadrado
Realizado por:	Admin
Fecha:	miércoles, 29 de octubre de 2014
Actualizando:	En vivo

	ZRES1		
Prueba Chi-cuadrado	zres1		
Media	0,0000		
Desviación estándar	0,9774		
Estadística Chi-cuadrado	59,7278		
Valor P	< 0.0001		
	6 - 1 ·	 - · · -	

Figure 43. Chi-Squared Goodness of Fit Test performed by Stat Tools for

Normality of Standardized Residuals generated by ANOVA Model through SPSS

The p-value is very small, being close to zero, and that means that the Normality Assumption has got to be rejected, nevertheless this fact does not mean automatically that the results obtained by ANOVA model are inacceptable ones.

Another strategy is to analyze the influence of factors over the severity of hip arthrosis one by one.

3.3.12.4 One Way Analysis:

Following the approach of Martínez-González, Miguel A. et al., (2009) the first step to perform in One Way ANOVA is to test the assumptions of the model. In this case the assumptions to be checked are those of "Normality" of Error Terms or Residuals of the model and "Homoscedasticity" or Homogeneity of Variances between groups of the sample.

a) Normality:

a.1. Comparison of three or more groups:

The Normality of the residuals is checked taking into account that the residuals of the model are calculated as the value of the current observation for dependent variable less the average of its group. In other words we would have to calculate the difference between every value of "Severity of hip arthrosis" and the average severity according to the sample "filtered" by, for instance, gender.

a.2. Comparison of two groups:

In case that the number of groups is less than three the most convenient procedure is to perform a "**T-Test Analysis**" which provides the same results that Analysis of Variance but with a lower degree of dependence on the assumptions of the model.

According to this kind of tests Normality assumption is met by default for samples over 30 elements. In case of having less than 30 elements any common "Normality test" can be performed, like Pearson "Goodness of Fit" Test, "Kolmogorov-Smirnov" Test, etc.

Another chance described by Martínez-González, Miguel A. et al., (2009) is to calculate deviation from "Normality" by comparing minimum and maximum values ,"Skewness" and "Curtosis" of the Residuals Frequencies Distribution with those of the "Standardized Normal Distribution", as follows:

- i. Range of values between $\mu \pm 3\sigma$, that is, the "residual" variable should not take values lower than its average less 3 times its standard deviation or higher than its average plus 3 times its standard deviation.
- ii. The skewness should not be greater than twice the standard error for asymmetry.
 - iii. The kurtosis should not be greater than twice the standard error for kurtosis.

b) Homoscedasticity:

b.1.Comparison of three or more groups:

This assumption can be checked through the "Levene Test" for homogeneity of variances which compares the biggest and smallest values reached for variance of dependent variable "filtered" by group of factor.

This comparison is performed through the ratio between smallest and biggest values of the variance of dependent variable, and this ratio is the experimental statistics to be compared with a Snedecor-Fisher Distribution, as follows:

F_{exp} =	Biggest Variance Smallest Variance	$\sim F_{n_1 - 1, n_2 - 1}$
(14)		

b.2. Comparison of two groups:

This assumption can still be checked by Levene Test but in case that the assumption of homoscedasticity is not fulfilled the T-Test can only still be performed with a correction of the "**degrees of freedom**", "DF", of the T-statistics according to "Welch Approximation":

$$DF = \frac{\left(\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}\right)^2}{\left(\frac{s_1^2}{n_1}\right)^2 + \left(\frac{s_2^2}{n_2}\right)^2}$$
(15)

Results:

A. Gender:

For this variable there is not "Normality" for the residuals of the model but since the sample size per each subgroup of the gender variable, "males" and "females", is bigger than 30 elements we assume that it is fulfilled according to the above mentioned.

Tests of Normality

		Kolm	ogorov-Smir	nov ^a	Shapiro-Wilk			
	GENDER	Statistic	df	Sig.	Statistic	df	Sig.	
RESULTS	1	,139	201	,000	,891	201	,000	
	2	,136	199	,000	,845	199	,000	

a. Lilliefors Significance Correction

Figure 44. Results of Normality Tests for Residuals of the model. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

> As it can be seen above the p-values of both Kolmogorov-Smirnov and Shapiro-Wilk Normality tests are not fulfilled in the slightest, giving both of them a zero p-value, since there is a big positive asymmetry.

Histogram

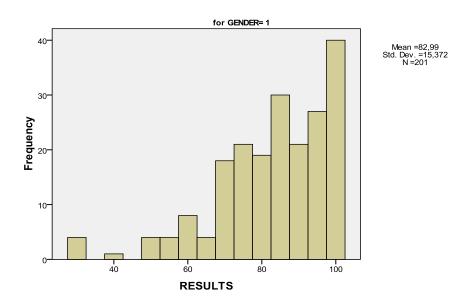


Figure 45. Frequencies Histogram of Results variable per subgroup of "males". Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The test of Homoscedasticity of subgroups is a "Levene Test" and the result is positive as we can see next:

Test of Homogeneity of Variances

RESULTS			
Levene Statistic	df1	df2	Sig.
,805	1	398	,370

Figure 46. Results of Levene Test for Homogeneity of Variances. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The p-value given by the test is very big and it is clearly above 5% significance level, therefore we accept that there is Homogeneity of Variances between men and women.

Both assumptions are fulfilled and it is possible to perform a parametric "T-test" for equality of averages validation.

		Levene's Test Varia	for Equality of nces		t-test for Equality of Means					
								95% Confidence Interval of the Difference		
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
RESULTS	Equal variances assumed	,805	,370	1,726	398	,085	2,859	1,657	-,397	6,116
	Equal variances not assumed			1,725	389,293	,085	2,859	1,658	-,400	6,119

Independent Samples Test

Figure 47. Results of T-Test for Subgroups Average Equality Validation. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The results obtained by SPSS show that the gender factor is not influencing the Severity of Hip Arthrosis, "Results" variable, since the p-value for "Equal variances assumed" option is over 0,05.

These results are in line with the preliminary results obtained with SPSS for the three ways with interactions ANOVA and for Cluster Analysis.

B. Kind of Arthrosis:

The assumption of Normality is considered to be fulfilled since the size of both subgroups, Type II and Type III Arthrosis, is over 30.

Homoscedasticity is not fulfilled since Levene Test gives negative results as it can be seen below:

Test of Homogeneity of Variances

RESULTS			
Levene Statistic	df1	df2	Sig.
18,494	1	398	,000

Figure 48. Results of Levene Test for Homogeneity of Variance according to Kind of Arthrosis Subgroups. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

Due to these results it is needed to use Welch approximation for setting the degrees of freedom of the "t" statistics.

		Levene's Test Varia			t-test for Equality of Means					
							95% Confidence Interval of the Difference			
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
RESULTS	Equal variances assumed	18,494	,000	8,556	398	,000	15,914	1,860	12,258	19,571
	Equal variances not assumed			6,545	102,910	,000	15,914	2,432	11,092	20,737

Figure 49. Results of T-Test for Average Equality Validation according to Kind of Arthrosis Subgroups. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

According to the results shown above on Figure above the averages of both kinds of Arthrosis are significatively different and it can be stated that the "Kind of Arthrosis" is really an influencing factor over the "Evolution" of Arthrosis as measured by the "Results" variable.

C. Age:

Since this factor consists of five categories labelled from A to E and ordered from lower to higher values it is not possible to perform a comparison of averages among groups through a T-Test.

This last technique is used for comparisons to be performed only between two subgroups as we have seen before and for comparing three or more groups we must use ANOVA Technique for parametric testing or Kruskal-Wallis test for nonparametric cases.

The circumstance that determines whether to use parametric or non-parametric methods is about fulfilment of assumptions of the model by the sample of data.

In case that assumptions are fulfilled parametric methods, like "Analysis of Variance", can be used, otherwise, non-parametric methods should be used in order to not get "inconsistent" estimates.

The first step is to check assumptions of the model:

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The assumption of Normality can be checked by calculating the "**residuals**" of the model, that is, the difference between the observed values of the dependent variable less the average of such variable along subgroups. In our case that will be performed by subtracting for every patient the sample average of "severity of hip arthrosis", filtered by the age subgroup, to the observed value, the real value, of severity for that patient.

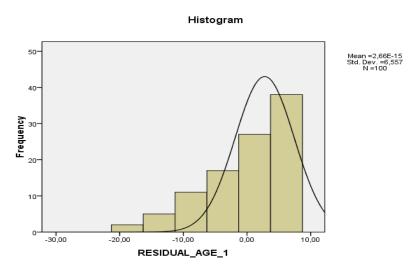


Figure 50. Results of T-Test for Average Equality Validation according to Kind of Arthrosis Subgroups. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

As it can be seen the residuals of the model for the first bracket of age, the youngest patients, has got a perfect positive asymmetry. This kind of asymmetry is extensive to the rest of brackets.

The overall results of Normality tests performed through SPSS are:

AGE RANGE	CATEGORY	MEAN Severity	K-S TEST
30-40	А	93,80	0,000
41-50	В	83,80	0,017
51-60	С	76,10	0,006
61-70	D	77,94	0,077
71-80	E	66,94	0,134

Figure 51. Results of Kolmogorov-Smirnov Normality Test for Residuals according to Age Subgroups. Source: Excel through SPSS output obtained with The Muscle-Joint Centre of Netherlands data.

According to these results for the p-values of the Kolmogorov-Smirnov "Goodness of Fit" Test there is only normality for those residuals related to the D and E subgroups, the oldest patients, which have been highlighted with red ink.

The conclusion is that "Normality" assumption is not fulfilled and we need to use non-parametric methods, like Kruskal-Wallis Test.

3.3.12.5 Kruskal-Wallis Test

The Kruskal–Wallis test is a nonparametric test to decide whether k independent samples are from different populations. Usually the decision between these alternatives is calculated by a one-way analysis of variance (ANOVA). But in cases where the conditions of an ANOVA are not fulfilled the Kruskal–Wallis test is an alternative approach because it is a nonparametric method; that is, it does not rely on the assumption that the data are drawn from a probability distribution (Usually a Normal Distribution).

The statistics used to perform the Kruskal-Wallis Test is based on Ranking the data, that is, considers grouping variable as an ordinal one, this statistics looks similar to Spearman Rank Correlation and its mathematical expression is as follows:

$$H = \frac{12}{N(N+1)} \sum_{j=1}^{k} \frac{R_j^2}{n_j} - 3(N+1)$$
(16)

Being:

H testing Statistics

N Overall Size sample

k Number of groups of the sample

 R_i^2 Square of Sum of ranks of j subgroup items

 n_i number of items of j subgroup

This H Statistics follows a χ^2 Pearson probability distribution with k - 1 degrees of freedom which values can be retrieved from a Table and given a significance level allows the researcher to set a "**Critical Value**", a threshold, to not be trespassed. So, in case that the H Statistics is bigger than this Critical Value the Null Hypothesis of the Kruskal-Wallis Test will be rejected with a mistake probability equal to the Significance Level of the test, meaning that the "**Medians**¹⁷" of all subgroups do not take the same value and these subgroups can be considered as coming from different populations. In reality the Statistics Inference part is exactly the same that for ANOVA Test, the main difference is about to work out the testing Statistics.

The results of this test, in case of being positive, will require to drive a final test between pairs. A Mann-Whitney test by couples of subgroups penalized by Bonferroni correction will need to be performed before setting what subgroups make the difference.

> Results:

The first is to set the fulfilment of the assumptions of the model.

The assumption of "Normality" is not needed in this non-parametric test, but there are some assumptions to be fulfilled on which the consistency of this technique relies:

- i. The subgroups have all the same probability distribution
- ii. There is homogeneity of variances among subgroups, that is, "Homoscedasticity"
- iii. It is supposed to exist "Independence" among observations.

¹⁷ This is another difference with respect to the ANOVA test, while ANOVA test performs a test for the equality of population averages among groups the Kruskal-Wallis test makes a comparison of "Medians" of the above mentioned groups instead of their averages.

We assume that the results of one patient do not depend on the results obtained by other patients and that assumption number iii is fulfilled.

To check "Homoscedasticity" we can do it as usual with a Levene Test:

Test of Homogeneity of Variances

RESULTS

Levene Statistic	df1	df2	Sig.
8,681	4	395	,000

Figure 52. Results of Levene Test for Homogeneity of Variances according to Age Subgroups. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The p-value obtained with Levene Test is zero and we can, therefore, reject the assumption of "Homoscedasticity".

There is another way of checking this assumption and it is by applying a test adapted to the non-parametric nature of the Kruskal-Wallis Test, as follows:

> i. First, since Kruskal-Wallis Test works with Ranks we will calculate a new variable which values will be the position of all observations of the "severity of hip arthrosis" dependent variable in the ranking.

- ii. Then we will calculate the average rank of the subgroup.
- iii. The difference between i and ii will be used to perform a One Way ANOVA Test which will set through the p-value obtained in this test the validity of "Homoscedasticity" assumption.

According to this approach the results obtained with SPSS are:

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1024326,02 9	4	256081,507	41,541	,000
Within Groups	2434982,79 7	395	6164,513		
Total	3459308,82 6	399			

ANOVA

Figure 53. Results of Analysis of Variance Test for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The decision is also to reject the assumption of Homoscedasticity according to the p-value given by SPSS in the last column of the ANOVA table.

Due to the fact that the data do not fulfil the assumptions of both ANOVA and Kruskal-Wallis Tests but that ANOVA test is a very "robust" technique in the sense that results obtained with different samples are not very different to each other, we will get the results given by ANOVA as the "true" ones. We will also confirm equality of results between ANOVA and Kruskal-Wallis Tests.

Test Statistics ^{a,b}				
-	RESULTS			
Chi-	142,118			
Square				
df	4			
Asymp.	,000			
Sig.				

a. Kruskal Wallis Test

b. Grouping Variable: AGE

Figure 54. Results of Kruskal-Wallis Test for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

According to the results obtained by this test the Age factor is influencing "severity of hip arthrosis", "Results" variable, and it can not be assumed that age subgroups have got all the same population average

And the results obtained by ANOVA Test through SPSS are of the same kind:

ANOVA

RESULTS

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	29607,798	4	7401,949	36,347	,000
Within Groups	80440,640	395	203,647		
Total	110048,438	399			

Figure 55. Results of ANOVA Test for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The last step following ANOVA Technique would be performing post-hoc analysis through the suitable test.

Since we have homoscedasticity of data by Age we will use as a post-hoc test called "Tamhane¹⁸" Test, which gives us the following results:

Multiple Comparisons

RESULTS Tamhane

Tallilate								
		Mean			95% Confide	ence Interval		
(I)	(J)	Difference (I-	Std.		Lower	Upper		
AGE	AGE	J)	Error	Sig.	Bound	Bound		
1	2	10,000*	1,553	,000	5,58	14,42		
	3	17,700 [*]	1,947	,000	12,15	23,25		
	4	15,859 [*]	2,548	,000	8,44	23,28		
	5	26,861 [*]	1,940	,000	21,23	32,50		
2	1	-10,000 [*]	1,553	,000	-14,42	-5,58		
	3	7,700 [*]	2,311	,010	1,15	14,25		
	4	5,859	2,836	,348	-2,30	14,01		
	5	16,861 [*]	2,305	,000	10,27	23,45		
3	1	-17,700 [*]	1,947	,000	-23,25	-12,15		
	2	-7,700 [*]	2,311	,010	-14,25	-1,15		
	4	-1,841	3,070	1,000	-10,62	6,94		
	5	9,161 [*]	2,588	,006	1,79	16,53		
4	1	-15,859 [*]	2,548	,000	-23,28	-8,44		
	2	-5,859	2,836	,348	-14,01	2,30		
	3	1,841	3,070	1,000	-6,94	10,62		
	5	11,002 [*]	3,065	,005	2,21	19,80		
5	1	-26,861*	1,940	,000	-32,50	-21,23		
	2	-16,861*	2,305	,000	-23,45	-10,27		
	3	-9,161 [*]	2,588	,006	-16,53	-1,79		
	4	-11,002 [*]	3,065	,005	-19,80	-2,21		

*. The mean difference is significant at the 0.05 level.

¹⁸ For further reading please see Martínez-González, Miguel A. et al., (2009).

Figure 56. Results of Post-Hoc Tamhane Test for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

According to these results the subgroups of age variable 1 and 5 are the most influencing ones since they give significative p-values for all comparisons with the rest of subgroups. This means that the youngest and oldest patients make the biggest differences

The groups 2, 3, and 4 are not so different to each other, they are different in terms of "severity of hip arthrosis" compared to groups 1 and 5, but group 4 seems not to be different in such sense of groups 2 and 3. This circumstance has been highlighted in red ink on the ANOVA table.

Finally an analysis of interactions between factors was performed, giving the following results:

Dependent Variable:RESULTS							
Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	
Corrected Model	41421,890 ^a	19	2180,099	12,072	,000	,376	
Intercept	1168629,431	1	1168629,431	6470,953	,000	,945	
AGE	15569,561	4	3892,390	21,553	,000	,185	
GENDER	446,836	1	446,836	2,474	,117	,006	
ARTHROSISKIND	3883,623	1	3883,623	21,504	,000	,054	
AGE * GENDER	670,768	4	167,692	,929	,447	,010	
AGE * ARTHROSISKIND	3425,543	4	856,386	4,742	,001	,048	
GENDER * ARTHROSISKIND	,014	1	,014	,000	,993	,000	
AGE * GENDER * ARTHROSISKIND	408,634	4	102,159	,566	,688	,006	
Error	68626,547	380	180,596				
Total	2771025,000	400					
Corrected Total	110048,437	399					

Tests of Between-Subjects Effects

a. R Squared = ,376 (Adjusted R Squared = ,345)

Figure 57. Results of Between-Subjects Test for all factors with ANOVA. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

3.3.13 Multivariate Logistic Regression:

3.3.13.1 Model Specification:

The model needs to be made of as many equations as categories of the dependent variable, "Severity of hip arthrosis", we have.

Therefore:

$$\log_{e} \frac{P_{i}^{1}}{P_{i}^{0}} = \beta_{10} + \sum_{h=1}^{H} \beta_{1h} X_{hi}$$
(17)
$$\log_{e} \frac{P_{i}^{2}}{P_{i}^{0}} = \beta_{20} + \sum_{h=1}^{H} \beta_{2h} X_{hi}$$
(18)

It will be the abridged version of our equation system to be solved in order to get the values of the explaining variables coefficients, β_{kh} .

We will include, initially, as many factors as those used in ANOVA model which will serve to two purposes:

- a. Validation of the ANOVA model: If we get similar relevant factors it will be like a double checking.
- ANOVA Models do not calculate the exact impact of factors over dependent variables while Logistic Regression Models do, so we can quantify the impact of every factor through the explaining

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variables coefficients, which are "Elasticities¹⁹" that measure the relationship between factors and the dependent variable.

The final model, replacing all theoretical parameters, by the real world variables, being:

 $\log_e \frac{P_i^1}{P_i^0} =$

 $\beta_{10} + \beta_{11}Age_i + \beta_{12}Gender_i + \beta_{13}ArthrosisKind_i + \beta_{14}Age *$ $Gender_i + \beta_{15}Age * ArthrosisKind_i +$ $\beta_{16}Gender * ArthrosisKind_i + \beta_{17}Age * Gender * ArthrosisKind_i$ (19)

 $\log_{e} \frac{P_{i}^{2}}{P_{i}^{0}} =$ $\beta_{20} + \beta_{21}Age_{i} + \beta_{22}Gender_{i} + \beta_{23}ArthrosisKind_{i} + \beta_{24}Age *$ $Gender_{i} + \beta_{25}Age * ArthrosisKind_{i} +$ $\beta_{26}Gender * ArthrosisKind_{i} + \beta_{27}Age * Gender * ArthrosisKind_{i}$ (20)

3.3.13.2 Regression Models:

A. Overall Regression:

¹⁹ Elasticity between two variables can be defined like the relative variation, variation percentage, over one of the variables after a relative variation of 1% in the other variable. From a mathematical point of view is equivalent to the slope of a curve in a point multiplied by the X and Y coordinates of that point. For further deepening in the concept please see Torres, F. (1996)

This technique works out the minimum quadratic distances from the data cloud to the Regression Line for all data of the sample as a whole. The main disadvantage of this technique is that does not take into account the differences for subgroups, that is, this technique is only suitable for those samples which have got a big homogeneity.

Special considerations need to be carried out since our data sample contains a lot of categorical independent variables, the factors of our model, which have got to be transformed into "dummy" variables of Boolean nature increasing the number of variables of such model.

The only pure quantitative independent variable or factor is "Age". "Number of Treatments" would also be a pure quantitative independent variable but its value has fixed to 7 for all patients becoming a constant or another assumption of the model.

Due to these circumstances the regression model in absence of "dummy" variables would be a univariate linear regression model, as follows:

$$\log_{e} \frac{P_{i}^{1}}{P_{i}^{0}} = \beta_{10} + \beta_{11} A g e_{i}$$
(21)

$$\log_e \frac{P_i^2}{P_i^0} = \beta_{20} + \beta_{21} Age_i$$
 (22)

Being P_i^0 , P_i^1 and P_i^2 the probabilities of a patient "i" to belong to the categories 0, 1, and 2, respectively. The base category is "C", in the denominator of the odd ratios, is set to zero, and it will correspond to a pain free level in the range of 0% to 70%.

Results:

Parameter	Estimates

									95% Confidence Interval for Ex (B)	
RE	ESULTS	S qualitative ^a	В	Std. Error	Wald	df	Sig.	Exp(B)	Lower Bound	Upper Bound
	А	Intercept	8,202	,809	102,700	1	,000			
		AGE	-,146	,015	96,119	1	,000	,864	,839	,890
	В	Intercept	3,599	,705	26,100	1	,000,			
		AGE	-,055	,012	22,384	1	,000	,947	,925	,968

a. The reference category is: C.

Figure 58. Results of Parameter Estimates for Logistic Regression for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The Wald Test for checking the assumption of coefficients of explaining variables being "zero" is significative, with a p-value of zero, meaning that both intercept and Age are relevant in this model.

The classical Pearson Linear Determination Coefficient from Linear Regression is replaced either by Pseudo-Coefficients that have not exactly the same meaning, or by a test of a ratio of likelihoods with and without all parameters.

The results of these tests are as follows:

Pseudo R-Square

Cox and Snell	,328
Nagelkerke	,372
McFadden	,185

Figure 59. Results of Pseudo R-Square tests for Logistic Regression for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

	Model Fitting Criteria	Likeli	hood Ratio 1	「ests
Effect	-2 Log Likeliho od of Reduce d Model	Chi- Square	df	Sig.
Intercept	451,571	176,999	2	,000
AGE	433,530	158,958	2	,000

Likelihood Ratio Tests

The chi-square statistic is the difference in -2 loglikelihoods between the final model and a reduced model. The reduced model is formed by omitting an effect from the final model. The null hypothesis is that all parameters of that effect are 0.

Figure 60. Results of Likelihood Ratio tests for Logistic Regression for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

Note that the top value for Pseudo R-Square of Cox-Snell is limited to 0,75. The Likelihood Ratio test is clearly significative with a p-value of 0. It seems that age is an influencing factor.

Finally to check the goodness of fit of the model to the data we will show the classification matrix obtained with SPSS:

Figure 61. Results of Classification Matrix for Logistic Regression for Age Factor. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

There are differences in classification according to the subgroup of severity of hip arthrosis, being the A subgroup, the patients with less pain, the subgroup with better fit.

The overall percentage of right classification according to classification matrix is not high, only a 55,5%, but we did not include the other factors yet.

B. Fixed Effects Model:

The "Fixed Effects" Model will include the dummy variables for every category of the categorical variables, that is, Gender and Kind of Arthrosis factors, as follows:

 $\log_{e} \frac{P_{i}^{1}}{P_{i}^{0}} =$ $\beta_{10} + \beta_{11}Age_{i} + \beta_{12}Gender_{i} + \beta_{13}ArthrosisKind_{i}$ (23)

 $\log_{e} \frac{P_{i}^{2}}{P_{i}^{0}} =$ $\beta_{20} + \beta_{21}Age_{i} + \beta_{22}Gender_{i} + \beta_{23}ArthrosisKind_{i}$ (24)

We do not need to include more than one dummy variable per factor due to the fact that these factors have only got two categories, but in another case the number of dummy variables to be introduced would be equal to the number of categories less one. In our case 2-1 = 1 dummy per factor.

Results:

The results obtained by this model are better than the previous ones with significative tests for all variables but the Gender variable, in this sense the outcome is in line with previous techniques, Cluster Analysis and Analysis of Variance, ANOVA.

	Model Fitting Criteria	Likeli	ihood Rat	io Tests			
Effect	-2 Log Likelihood of Reduced Model	Chi- Square	df	Sig.			
Intercept	490,665	63,800	2	,000			
AGE	548,317	121,451	2	,000			
GENDER	427,609	,744	2	,689			

Likelihood Ratio Tests

ARTHROSISKI	449,070	22,205	2	,000
ND				

The chi-square statistic is the difference in -2 log-likelihoods between the final model and a reduced model. The reduced model is formed by omitting an effect from the final model. The null hypothesis is that all parameters of that effect are 0.

Figure 62. Results of Likelihood Ratio Tests for Logistic Regression for Age, Gender and Kind of Arthrosis Factors. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

								95% Confidence Interval for Exp(B)	
			Std.					Lower	Upper
RESULTS qualitative ^a		В	Error	Wald	df	Sig.	Exp(B)	Bound	Bound
А	Intercept	6,378	,907	49,403	1	,000			
	AGE	-,135	,015	76,768	1	,000	,874	,848	,901
	GENDER	,271	,326	,691	1	,406	1,311	,692	2,483
	ARTHROSISKI	1,471	,396	13,827	1	,000	4,354	2,005	9,455
	ND								
В	Intercept	1,925	,811	5,632	1	,018			
	AGE	-,044	,012	12,593	1	,000	,957	,934	,981
	GENDER	,211	,293	,516	1	,473	1,235	,695	2,194
	ARTHROSISKI	1,354	,321	17,799	1	,000	3,872	2,064	7,261
	ND								

Parameter	Estimates
I alameter	Loundleo

a. The reference category is: C.

Figure 63. Results of Parameter Estimates for Logistic Regression for Age, Gender and Kind of Arthrosis Factors. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

As it can be seen above all tests give very low p-values, resulting in very significative tests, but for Gender factor whose results we have highlighted in red ink. Even the residuals seem to have "Normality", note that residuals in this kind of regression are calculated in a different way compared to Classical Regression Models. Pearson found out a way of checking this assumption with a coefficient that works in a similar way to his well-known "**Goodness of Fit**" coefficient, that is, working out the square differences between observed and expected values.

"Homoscedasticity" does not need to be checked since Logistic Regression is a heteroscedastic model by default.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	278,025	256	,165
Deviance	287,097	256	,088

Figure 64. Results of Goodness of Fit Test for Logistic Regression for Age, Gender and Kind of Arthrosis Factors. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

Finally, the Classification matrix is as follows:

	Predicted				
Observed	A	В	С	Percent Correct	
А	128	37	4	75,7%	
В	50	63	24	46,0%	
С	14	30	50	53,2%	
Overall Percentage	48,0%	32,5%	19,5%	60,3%	

Classification

Figure 65. Results of Classification matrix for Logistic Regression for Age, Gender and Kind of Arthrosis Factors. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

According to the Classification Matrix output the model seems to fit a little bit better with the effect of the three factors altogether, but the mistakes still go in the same direction, A is the best fitted subgroup and B the worst.

3.3.14 Multivariate General Regression:

3.3.14.1 Model Specification:

Due to the values set for SPSS "Results" variable, "Severity of Hip Arthrosis" variable, maybe it is not possible to perform this kind of analysis since in spite of looking like a continuous variable it only gets a few values, so the values taken by this variable may be are not suitable for a quantitative regression.

To confirm this point we generated some graphs with SPSS. The results can be seen next:

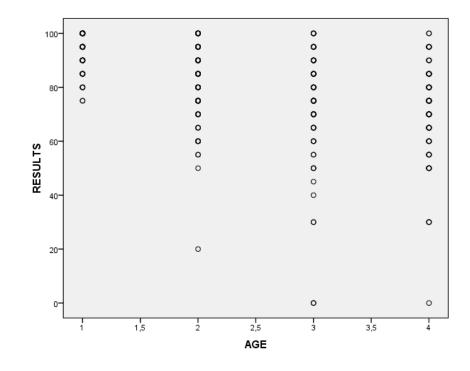


Figure 66. Scatter plot between Age and Results. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

This is the way the relationship between "Severity of Hip Arthrosis" and "Age" looks like, being this relationship the most quantitative one it means that it is not possible to perform a quantitative regression for our research. Note that it would be possible in case that there is a refinement in the measurement of the dependent variable that makes it measure the degree of severity of hip arthrosis in a more accurate way.

3.3.15 Discriminant Factorial Analysis:

According to previous techniques we already know that the "Normality" assumption is not fulfilled.

As for "Homoscedasticity" assumption a "Global Multivariate Homoscedasticity Test" can be performed through this technique for all independent variables, factors, as a whole. This is performed through the Box's M test which results are as follows:

Test Results

Γ	Box's M		53,593
	F	Approx.	4,414
		df1	12
		df2	474190,872
		Sig.	,000

Tests null hypothesis of equal population covariance matrices.

Figure 67. Results for Box' M Test for Global Multivariate Homoscedasticity. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

The results are in line with our previous findings, that is, there is no "Homocesdasticity" considering all variables as a whole. This is pretty logical considering that there was no homocesdasticity for any variable, as Levene' test proved before.

These circumstances, altogether, may lead to inconsistencies in the estimates reached through the different techniques. This will be shown with the Classification matrix obtained by SPSS.

The interest of applying several techniques is to compare results and to get common conclusions in spite of the lack of fulfilment of the model assumptions by the sample data.

In that sense the "Discriminant Function" results are as follows:

	Function		
	1	2	
AGE	,859	,559	
GENDER	-,062	,032	
ARTHROSIS KIND	-,357	,954	

Standardized Canonical Discriminant Function Coefficients

Figure 68. Results for Box's M Test for Global Multivariate Homoscedasticity. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

	Function		
	1	2	
AGE	,934	,355	
ARTHROSIS KIND	-,545	,836	
GENDER	-,061	,104	

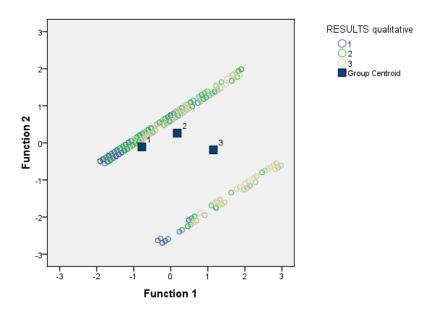
Structure Matrix

Figure 69. Results for Structure Matrix.

Source: SPSS through The Muscle-Joint Centre of Netherlands data.

It can be seen in both graphs above that the gender factor is the least important among all and, in this sense, the conclusions are in line with previous results obtained with Clusters Analysis, Analysis of Variance and Logistic Regression. In spite of all possible limitations set by the lack of fulfilment of the assumptions of the above mentioned techniques it seems clear that Age is the most influencing factor, then Kind of Arthrosis is second and Gender is the least influencing among all factors. Interactions among these factors have to be analyzed deeply on further analysis to be performed in this research.

The Discriminant Functions with the centroids, that is, the averages, of every group or category of the "Severity of Hip Arthrosis" dependent variable being like this:



Canonical Discriminant Functions

Figure 70. Canonical Discrimination Functions Plot. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

And finally the Classification Matrix is:

		RES ULTS	Pre N				
		qualit ative	1	2	3	Total	
Original	Count	1	120	40	9	169	
		2	48	59	30	137	
		3	12	25	57	94	
	%	1	71,0	23,7	5,3	100,0	
		2	35,0	43,1	21,9	100,0	
		3	12,8	26,6	60,6	100,0	
Cross-	Count	1	120	40	9	169	
validated ^a		2	48	58	31	137	
		3	12	27	55	94	
	%	1	71,0	23,7	5,3	100,0	
		2	35,0	42,3	22,6	100,0	
		3	12,8	28,7	58,5	100,0	

Classification Results^{b,c}

a. Cross validation is done only for those cases in the analysis. In cross validation, each case is classified by the functions derived from all cases other than that case.

b. 59,0% of original grouped cases correctly classified.

c. 58,3% of cross-validated grouped cases correctly classified.

Figure 71. Classification Matrix. Source: SPSS through The Muscle-Joint Centre of Netherlands data.

Note that it is still the category of the youngest patients that which is better classified and the category of the oldest ones that which is worse classified.

3.3.15.1 Literature Review:

BIRMINGHAM, T. B. (2009). *Medial Opening Wedge High Tibial* Osteotomy: A Prospective Cohort Study of Gait, Radiographic, and Patient-Reported Outcomes. Arthritis & Rheumatism (Arthritis Care & Research) Vol. 61, No. 5, May 15, 2009, pp 648–657:

In this research a cohort of patients are followed after osteotomy of wedge high tibial according to a triple control:

- a. Gait
- b. Radiographic Control
- c. Patient-reported Outcomes

This follow up process is statistically supported by a Cluster Analysis and a General Multivariate Linear Regression.

The "Cluster Analysis" has got the following features:

- ii. Technique: 2-Step Hierarchical Clustering Model
- iii. Similarity Index: Euclidean Distance
- iv. Goodness of Fit: Akaike's Information Criterion
- v. Exclusion of Analysis: Control by Outliers not included in any cluster.
- vi. Post-Hoc Analysis between Clusters:
 - Independence T-Tests
 - Wilcoxon's Rank Sum Test
 - Pearson Chi-square Test

After creating the clusters a "**Multivariate Linear Regression**" analysis was performed reaching a 43% of common causes between 2 years post-operative changes and explaining variables.

The results obtained after this analysis are that only two clusters were created as for the way "joint-weight load" and "knee pain" were related to changes in "pain scores" dependent variable, but no other factors could be found among demographic or clinical ones.

BYERS, P. D. y GLENNIE, B. . (1975). Attempt to classify patients with arthritis of the hip suitable for prosthetic replacement, and their femoral heads. Annals of the Rheumatic Diseases, 34, 298-302:

On this research the authors tried to fit data obtained from bone heads of hip joints for patients with osteoarthritis of the hip after replacement by prostethic ones. They attempted to set standards on bone head features in order to link them to sickness evolution.

In spite of careful scientific procedure for getting the right bone heads in similar medical conditions the results obtained after applying two statistical multivariate techniques, namely "Cluster Analysis" and "Discriminant Factorial Analysis", were not satisfying ones making researchers think of OsteoArthritis like a "*Spectrum of Disease*" that can not be assessed by conventional statistical analysis.

As the authors remind in their article:

[...." It is commonplace now to regard the pathogenesis of osteoarthrosis as complex, with a range of possible starting points and routes. Kellgren (1961) hypothesized that osteoarthrosis is a mixture of diseases....."]

And as the authors keep saying in their own words:

[...."A selection of several different types of cluster analysis were chosen from a suite called Clustan (Wishart, 1972). However, no consistent groupings were formed by the cluster analyses...."]

To keep saying:

[...." Subsequent to the failure of cluster analysis to formulate any meaningful classification of arthritis, it was suggested that the data should be subjected to a discriminant analysis. A Stepwise Discriminant Analysis program was used-BMDO7M (1971 revision)"]

And:

[...." The most striking finding is that the analyses failed to provide consistent and definitive discrimination between the groups...."]

Murphy, S. L. et al. (2011). Subgroups of older adults with osteoarthritis based upon differing comorbid symptom presentations and potential underlying pain mechanisms. Arthritis Research & Therapy 2011, 13:R135:

This research tries to make groups of patients with OsteoArthritis according to different comorbidities.

For that purpose the researchers used two statistical techniques:

a. Hierarchical Agglomerative Cluster Analysis:

To create the profiles of the patients according to their different features in relation to their OA sickness. b. Multiple Analysis of Variance (MANOVA):

To measure the individual relative contribution of each variable, Factor, to the belonging Cluster.

The conclussions obtained with this research were that three clusters were built according to the values of dependent variable, which was formed by indicators like "Mood", "Fatigue", "Illness Burden", "Sleep problem" and "Functional Status", but no evidence was found for either clinical or demographic factors influence over such dependent variable.

According to their own words:

[...."Clinical and demographic variables among subgroups Age did not differ across clusters (mean = 72 years; F(2,122) = .036, P = .97), and there was no significant relationship between gender and cluster assignment (c2 = 3.72, P = .16). Similarly, body mass index (BMI) did not differ across clusters, being within the category of obese (for example, 30 to 31) on average (F(2,122) = 1.02, P =.36). With regard to OA joints per the ACR clinical criteria, we examined the clusters according to whether they had knee OA alone or whether OA was in both the hip and knee or in the hip joints alone. The most prevalent group in all clusters had knee OA alone (82% in Cluster 1, 64% in Cluster 2, and 63% in Cluster 3); however, location of OA joint was not significantly different across clusters...."]

Otterness, I. G. et al. (2000). An analysis of 14 molecular markers for monitoring osteoarthritis: segregation of the markers into clusters and distinguishing osteoarthritis at baseline. Osteoarthritis and Cartilage (2000) 8, 180–185: This research is about to link biomarkers to some categories according to their properties within the context of Osteoarthritis Research.

The techniques used for this purpose were:

- a. Clusters randomized clinical trials
- b. Discriminant Factorial Analysis
- c. Logistic Regression
- d. Main Components Analysis

After sampling data by "a" it was clear that there was a "Non-Normal" probability distribution for explaining variables data and, therefore, a logarithmic transformation had to be applied to them in order to reach "Normality".

The kind of average used to summarize information about the sample was a geometric average instead of an arithmetic one. These averages had to be compared through non-parametric techniques, like "Wilcoxon Rank Sum Test", the equivalent to "Kruskal-Wallis" Test when the number of samples to be compared is less than two.

<u>Tejedor Varillas, A. et al. (2012). Can an intervention on clinical inertia have an impact on the perception of pain, functionality and quality of life in patients with hip and/or knee osteoarthritis?</u> <u>Results from a cluster randomised trial. Aten Primaria.</u> <u>2012;44(2):65-73:</u>

In this Research a Cluster Randomized Trial was used to create two groups of patients according to the training of staff who took care of them for reinstatement purposes. One group was that of patients whose physical therapists had been trained for skipping "clinical inertia" and the other group was that of patients whose physical therapists kept working as usual. The results of this experiment were measured on a set of indicators which were aggregated to compound an only dependent variable. These indicators were:

- a. Pain
- b. General Health
- c. Vitality
- d. Social Functioning

The explaining variables or factors that contributed to the value taken by the dependent variable were:

- a. Physical Functioning
- b. Physical Role
- c. Emotional Role
- d. Mental Health

The conclusions obtained by this research were that there were no differences in the health of both groups of patients, the only difference found was about "vitality" from those patients who were cared by physical therapists with a training course in "Stopping Clinical Inertia". Sulsky, S.I., Carlton, L., Bochmann, F., Ellegast, R., Glitsch, U., et al. (2012) Epidemiological Evidence for Work Load as a Risk Factor for Osteoarthritis of the Hip: A Systematic Review.PLoSONE7(2):e31521.doi:10.1371/journal.pone.003152 1:

This research is focused on literature review of the association between physical work and Hip Osteoarthritis.

The authors chose a final sample of 6 valid researches to set some conclusions. These researches had the right quantitative approach and good quality of data as well. The evaluation was performed by a team of epidemiologists.

A brief summary about the state of the art on incidence and prevalence rates split by risk factors is included in the scope of this study, whose main conclusions are as follows:

- a. Hip Osteoarthritis (OA) Risk Factors:
 - i. Genetic Predisposition
 - ii. "Previous" Arthritis of the knee and finger joints: They consider specially relevant this factor in confluence with being woman, so there is some kind of interaction between "gender" and "other arthritis" factors, which increase exponentially the risk to get sick with Hip OA.
 - iii. Malformations of Hip, Hip Dysplasia or Femoroacetabular Impingement
 - iv. Demographic Factors such as "Race" or "Gender"

- v. Systemic Factors: Obesity or Metabolic Disorders
- vi. Sports: Long Distance Running
- vii. Occupational Factors such as "Farming" or "Heavy Physical Work Load"
- b. Markers:

The subgroups with more risk are those aged between 70 and 79 years old and women.

c. Association between Physical work and Hip OA:

The final sample of good quality researches chosen as literature review agreed on setting a causal relationship between physical work and Hip OA.

Castaño Carou, A. (2014). Evaluación clínica del paciente con artrosis. Estudio multicéntrico nacional "EVALÚA". Tesis Doctoral. La Coruña: UDC:

This Research is a Dissertation that tries to get a picture of the profile of the patient affected by Hip Osteoarthritis.

The tool used for this purpose is a combination of both Literary Review and Questionnaires filled by patients who are users of the services of Spanish Social Security located in Galicia

The aim of this research is to confirm figures provided by International Literature about the subject. There is not a quantitative background to give statistical support to the dissertation as the author says on several ocassions. The main conclusions obtained were:

- a. Gender is a risk factor to get sick with arthrosis of any kind: knee, hip, hands, etc. Women are more suitable to develop this sickness than men.
- b. Age is another important risk factor and according to the author of the dissertation there is an interaction between Age and Gender increasing exponentially the risk of getting sick with hip OA.
- c. Obesity is also an important risk factor. There is some evidence on International Literature about the subject explaining that this factor could be related to the osteophytes progression and to the increase of incidence rates and to the decrease of joint space.

Autor	Año	Lugar	Localización artrosis	n	Mujeres	Hombres				
Estudios en pacientes con artrosis										
Creamer(108)	2000	USA	Rodilla	69	69,60%	30,40%				
Ethgen(120)	2002	Bélgica	Rodilla y cadera	108	86,10%	13,90%				
Rejeski(121)	2002	USA	Rodilla	316	71,97%	28,03%				
Salaffi(96)	2005	Italia	Rodilla	244	62,8%	37,2%				
			Cadera		55,1%	44,9%				
Batlle(88)	2006	España	Rodilla	1071	76%	24%				
			Cadera		66%	34%				
Whitfield(92)	2006	Australia	Artrosis	222	67%	33%				
Jordan(100)	2007	USA	Rodilla	3018	57,40%	42,60%				
Escobar(110)	2007	España	Rodilla	516	75%	25%				
Escobar(111)	2007	España	Rodilla	640	73,60%	26,40%				
Gaudet(113)	2007	Canadá	Cadera	161	63,40%	36,60%				
Hutchings(116)	2007	USA	Rodilla y cadera	287	70%	30%				
Núñez(104)	2008	España	Rodilla	100	71%	29%				
Chan(102)	2009	China	Rodilla	455	70%	30%				
Debi(106)	2009	Israel	Rodilla	134	64%	36%				
Desmeules(109)	2009	Canadá	Rodilla	197	64%	36%				
Escobar (112)	2009	España	Rodilla y cadera	684	62%	38%				
Reeuwijk(94)	2010	Holanda	Rodilla y cadera	288	71,20%	28,80%				
Ambrose(105)	2010	Irlanda	Rodilla	96	64%	36%				
Basaran(107)	2010	Turquía	Rodilla y cadera	117	Rodilla: 90%	Rodilla: 10%				
					Cadera: 82%	Cadera: 18%				
Grindrod(114)	2010	Canadá	Rodilla	124	64%	36%				
Martin(123)	2010	España	Artrosis	135	67,40%	32,60%				
Hawker(115)	2011	Canadá	Rodilla y cadera	529	78,50%	21,50%				
Loza(117)	2011	España	Rodilla	226	75%	25%				
Cordero-	2012	España	Artrosis	965	75%	25%				
Ampuero(91) Laclériga(126)	2012	España	Rodilla	1386	68%	32%				
Racaza(93)	2012	Filipinas	Artrosis	859	74,5%	25,5%				
EVALÚA	2007	España	Rodilla, cadera y manos	1258	77,8%	22,2%				

Tabla 56. Prevalencia de artrosis según el género en diferentes estudios (II)

Figure 72. Athrosis prevalence grouped by gender on International Literature. Source: Castaño Carou, A. (2014)

3.4 DISCUSSION:

A lot of different statistical techniques and methods have been applied through this dissertation which sometimes gave different results due to the lack of fulfilment of basic assumptions by sampled data. A summary of such results are shown next:

			ASSUMPTIONS			RESULTS		
METHOD	FACTOR	TECHNIQUE	KIND	TEST	FULFILLED ?	A priori TEST	P- VALUE	SIGNIFICATIV ENESS
ANOVA	Gender	T-Test	Normality	Big Sample	Y			
			Homoscedasticity	Levene	Y	T-Test Approx. Welch	0,085	N
	ArthrosisKind	T-Test	Normality	Big Sample	Y			
			Homoscedasticity	Levene	N	T-Test Approx. Welch	0,000	Y
	Age	One Way ANOVA	Normality	K-S	Ν			
			Homoscedasticity	Levene	N	F-Test	0,000	Y
		Kruskal- Wallis	Homoscedasticity	Levene	N	Chi-squared Test	0,000	Y
	Gender*Age	Factorial ANOVA	Normality	K-S	N			
			Homoscedasticity	Levene	N	F-Test	0,447	N
	Gender*Arthros isKind	Factorial ANOVA	Normality	K-S	N			
			Homoscedasticity	Levene	N	F-Test	0,993	N
	Age*ArthrosisKi nd	Factorial ANOVA	Normality	K-S	N			
			Homoscedasticity	Levene	N	F-Test	0,001	Y
	Gender*Age*Ar throsisKind	Factorial ANOVA	Normality	K-S	N			
			Homoscedasticity	Levene	N	F-Test	0,688	Ν
CLUSTER ANALYSIS	Gender	2-Steps	-	-	-			High impact but Inconsistent
	ArthrosisKind	2-Steps	-	-	-			Irrelevant
	Age	2-Steps	-	-	-			Irrelevant
DISCRIMIN ANT FACTORIAL ANALYSIS	Gender	Canonical Correlations	Normality	K-S	N	Wilks' Lambda	0,001	Low Impact but Inconsistent
			Homoscedasticity	Box's M	N			

	ArthrosisKind	Canonical Correlations	Normality	K-S	Ν	Wilks' Lambda	0,001	Medium Impact but Inconsistent
			Homoscedasticity	Box's M	N			
	Age	Canonical Correlations	Normality	K-S	Ν	Wilks' Lambda	0,001	Medium Impact but Inconsistent
			Homoscedasticity	Box's M	N			
LOGISTIC REGRESSIO N	Gender	Maximum Likelihood through Newton- Raphson Algorithm	Normality	K-S	Ν	Log Ratio of Likelihoods	0,689	Ν
	ArthrosisKind	Maximum Likelihood through Newton- Raphson Algorithm	Normality	K-S	Ν	Log Ratio of Likelihoods	0,000	Y
	Age	Maximum Likelihood through Newton- Raphson Algorithm	Normality	K-S	Ν	Log Ratio of Likelihoods	0,000	Y
	Gender*Age	Maximum Likelihood through Newton- Raphson Algorithm	Normality	Pearson	Ŷ	Log Ratio of Likelihoods	0,001	Y
	Gender*Arthros isKind	Maximum Likelihood through Newton- Raphson Algorithm	Normality	Pearson	Y	Log Ratio of Likelihoods	0,000	Y
	Age*ArthrosisKi nd	Maximum Likelihood through Newton- Raphson Algorithm	Normality	Pearson	Y	Log Ratio of Likelihoods	0,086	N
	Gender*Age*Ar throsisKind	Maximum Likelihood through Newton- Raphson Algorithm	Normality	Pearson	Y	Log Ratio of Likelihoods	0,000	Y

Figure 73. Summary of Results obtained with SPSS through different Techniques and Methods. Source: Own design through Excel.

These results present inconsistency giving different figures from one technique to another. But there are also some similarities which cannot be the result of just a "lucky chance", as follows:

d. The gender is not considered relevant "without inconsistencies" by any of the techniques used in this dissertation. In our random sample sex was not proven to be relevant. This could be due to the randomness of the sample, the fact that the patient are mostly from a higher social economic class (i.e.: most patients chose to receive treatment in the clinic themselves), they are not sent by the general physician.

Thus no gender relevance could be affected by the fact that most of these patients are or participate in managerial-executive type function that involves more sitting thus more shortening of the iliopsoas with eventual more pressure in the femur-acetabular joint over many years.

- e. The Age and Kind of Arthrosis are considered relevant factors "without inconsistencies" by ANOVA and Logistic Regression Methods and relevant "with inconsistencies" by Cluster Analysis and Discriminant Factorial Analysis. Age is relevant because the longer the compression forces from the iliopsoas are present the more intra articular damage is done.
- f. Interactions, which are only worked out by ANOVA and Logistic Regression methods give place to the highest inconsistencies among all:

All interactions in which "Gender" factor is included are considered irrelevant, not significative, by ANOVA, while they are considered relevant by Logistic Regression.

For the remaining interaction, "Age*Arthrosis Kind", it happens the same, but in the opposite direction, ANOVA considers it relevant and Logistic Regression irrelevant.

There is doubt of the reliability of data supplied in our study, because this is not really a sample of the general population. The patients from this Centre chose themselves for this treatment (i.e.: not after referred by physician).

The different statistical methods and techniques used in this dissertation have different features, and due to the general lack of fulfilment about the basic assumptions of the models, those methods and techniques with a lower dependency on such assumptions would be more accurate and reliable on their results.

On the other hand a less dependency on some assumptions, that is, on some statistical features, does not guarantee a better fitting of the model to the data.

4 CHAPTER III

5.1 RESEARCH QUESTIONS

After the statistical analysis and the literature review the following questions arise:

- I. How can be set the influencing factors over Hip Osteoarthritis?
- II. What statistical tools could help the researcher to get consistent estimates?

5.2 CONCLUSSIONS

There are several researches that did not find any evidence from "**demographic**" data of patients with Hip Osteoarthritis as to set a link between those factors and the evolution of severity of Hip Arthrosis.

Some of the authors of these researches were absolutely amazed by this fact and could not find a scientific explanation for it. For instance, Byers, P. D. and Glennie, B., (1975) referred to Osteoarthritis as a "Spectrum of Disease" in the sense of the complexity of factors involved in this subject.

These findings happened in recent times as well, like in Birmingham, T. B., (2009) and in Murphy, S. L. et al. (2011) with no less surprise by these authors.

Recent studies, like one from 2014, Castaño Carou, A.I., (2014), have reviewed the literature about Hip OA factors, finding that gender was a clear factor for getting any kind of Arthrosis, including those related to Hips. In this sense women were much more likely to get sick with Osteoarthritis than men, although these were more likely to get sick with Hip Osteoarthritis than with knees Osteoarthritis, which was the most likely kind of osteoarthritis to be developed by women.

Age was also found like a relevant factor for developing Hip OA, specially in the range of 70 to 79, bracket in which there was an exponential growth in the number of new cases, "incidence", of Hip OA among the elders.

There was also interaction between age and gender, according to previous studies that were reviewed by Castaño Carou, although she did not perform any powerful statistical tool to check this circumstance.

Related to improvements in the "**statistical analysis**" there are references in the International Literature about this subject referring to logarithmic transformation in explaining variables to try to reach "Normality", that is, a "Bell" shape in the frequency distribution of data.

Accompanying the "log" transformation of data should go the use of geometric averages instead of arithmetic ones in order to be able to perform "efficient" and "consistent" averages comparison among populations. Our data presented with a big asymmetry and these transformations could help to fix a little bit this asymmetry in order to reach "Normality".

Another question is about "Homoscedasticity" which could never be fulfilled in any of the tests performed to the sample of patients. No concrete recommendations were found on the literature review of this subject, although quadratic discrimination functions instead of linear ones could help to improve consistency of Discriminant Factorial Analysis, which has missclasified a lot of our data, reaching a very low "success" rate.

This "success" rate should give the same figure, exactly the same, in case of a consistent "analysis" by this technique, that the one obtained through "Logistic Regression". Differences are due to the lack of fulfilment of the basic assumptions of the model by the sampled data.

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Due to the strong "Homoscedasticity" in our data, bigger even than the Non-Normality, the most reliable conclussions should be those reached by Logistic Regression since this technique does not rely on Homoscedasticity of data, being always heteroscedastic by default given the mathematical nature of the model. These conclussions are partly in line with the recent literature review which considers the interaction of Gender and Age as significative, although our research results show no relevance for Gender as a stand-alone factor.

These conclussions reached by Logistic Regression model are focused on the state of Hip Ostearthritis at a time for a given patient with some specific features about gender, age and kind of arthrosis, but the evolution of severity of Hip Arthrosis can not be set by this procedure, needing measurements from two different time points in order to be able to fix the difference between one point and another.

Patients in this Center chose this treatment themselves in a higher level of health awarness that the typical patient found in a hospital setting. In other words these patients were proactive in there desire to stop hip replacement surgery.

Within this dissertation we have the following:

- 1) Patients who choose this examination and treatment methods themselves
- Evaluation of the hip joints both on radiograph and palpatory orthopedic test examination
- Evaluation of the most likely cause of the hip degeneration namely the shortened or contracted lliopsoas muscle.
- Determiny the extent of the Iliopsoas shortening through examination procedure.
- After 7 treatments evaluating the patients subjective responce to this treatment.

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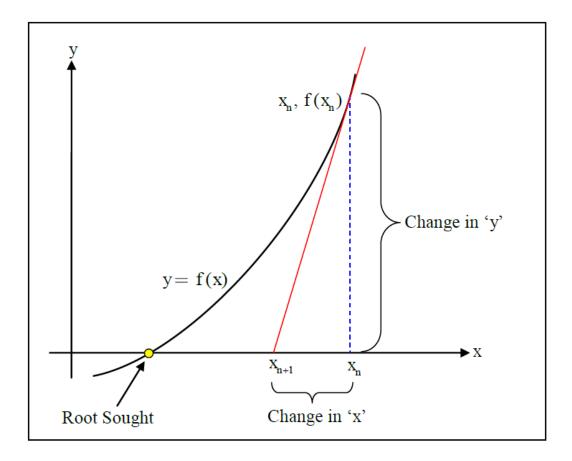
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5.4 ANNEXES

5.4.1 NEWTON-RAPHSON ALGORITHM:



The Newton-Raphson method is based on the principle that if the initial guess of the root of f(x) = 0 is at x_i , then if one draws the tangent to the curve at $f(x_i)$, the point x_{i+1} where the tangent crosses the *x*-axis is an improved estimate of the root (Figure 1).

Using the definition of the slope of a function, at $x = x_i$

$$f'(x_i) = \tan \theta$$
$$= \frac{f(x_i) - 0}{x_i - x_{i+1}},$$

which gives

$$x_{i+1} = x_i - \frac{f(x_i)}{f'(x_i)}$$
(1)

Equation (1) is called the Newton-Raphson formula for solving nonlinear equations of the form f(x)=0. So starting with an initial guess, x_i , one can find the next guess, x_{i+1} , by using Equation (1). One can repeat this process until one finds the root within a desirable tolerance.

Algorithm

The steps of the Newton-Raphson method to find the root of an equation f(x) = 0 are

- 1. Evaluate f'(x) symbolically
- 2. Use an initial guess of the root, x_i , to estimate the new value of the root, x_{i+1} , as

$$x_{i+1} = x_i - \frac{f(x_i)}{f'(x_i)}$$

3. Find the absolute relative approximate error $|\epsilon_a|$ as

$$\left|\epsilon_{a}\right| = \left|\frac{x_{i+1} - x_{i}}{x_{i+1}}\right| \times 100$$

4. Compare the absolute relative approximate error with the prespecified relative error tolerance, \in_s . If $|\in_a| > \in_s$, then go to Step 2, else stop the algorithm. Also, check if the number of iterations has exceeded the maximum number of iterations allowed. If so, one needs to terminate the algorithm and notify the user

5.4.2 EVOLUTION OF ARTHROSIS:

