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EVALUATION OF GENETIC MARKERS IN ATHLETES AND PATIENTS WITH CARTILAGE INJURY AND OSTEOARTHRITIS NON-RESPONSIVE TO CONSERVATIVE TREATMENT – METHODS DESCRIPTION

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Disclosure:

The authors declare that they have no conflict of interest.

Cartilage injuries and Osteoarthritis

Cartilage injuries and Osteoarthritis are a public health problem due to population senescence, causing pain, functional limitations and high treatment costs.

(Perera, Gikas, and Bentley 2012; Flanigan et al. 2010)

Genetic studies can help to identify the biological processes that are involved in the induction of these lesions and, consequently, potential therapeutic targets.

(Gomoll et al. 2010; Showery et al. 2016)

Single Nucleotide Polymorphisms (SNPs) are common forms of genetic variation in the population and genome-wide association studies (GWAS) are known to accelerate the localization of genes associated with diseases of multifactorial and complex inheritance as OA.

(Wang et al. 2016)

Recent studies have shown a correlation between SNPs and OA.

Aubourg G et al. (2021)

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Aim:

The present study aims to describe the genetic markers most related to worse prognosis and clinical outcomes for cartilage injury and osteoarthritis.

Methods Description

This is a pilot study for cross-sectional evaluation of patients with symptomatic chondral lesions and osteoarthritis undergoing conservative treatment and without clinical improvement.

Spittle samples were collected using the Genera® kit and DNA extracted according to the manufacturer's protocol, being quantified using a microarray technique.

Athletes and patients non-responsive for conservative treatment were clinically evaluated by PROMS regarding pain and function.

The assessments were complemented with radiography and magnetic resonance imaging.

Patients were classified and included as non-responsive and, therefore, requiring surgical treatment.

Methods Description

Inclusion Criteria

Patients between 18 and 65 years old, BMI below 30, with cartilage damage and knee osteoarthritis who do not respond to non-operative therapy with a minimum follow-up period of 6 months and indication for surgical treatment and patients with knee osteoarthritis who respond to conservative therapy and known clinical response without indication for surgical treatment

Exclusion Criteria

Patients who do not want or are not able to consent to their participation in the research through the TCLE. Those patients who requested to stop the study.

Methods Description

Patient evaluation

Assessed by subjective International Knee Documentation Committee (IKDC) outcome scores, Lysholm Knee Score, Knee injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analogue Score (VAS) and Short Form-36 (SF-36).

Sample size

75 samples from the group that responded to conventional treatment for OA will be compared with 75 samples from the group that did not respond to conventional treatment for OA, based on previous studies that used 50 to 350 samples in the experimental group.

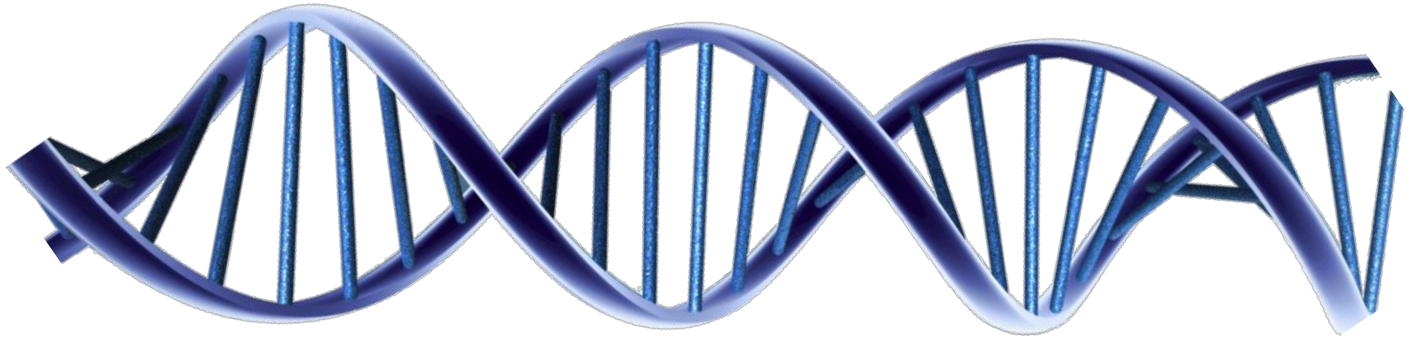
(n = 50 (Diab et al. 2017), n = 350 (Zhang et al. 2018), mn = 267 (Meulenbelt et 2008).

Methods Description

Genotyping

SNPs or genes previously associated with cartilage damage and osteoarthritis will be evaluated. Genotyping will be performed with the single nucleotide polymorphism (SNP) microarray (GSA 750K). Infinium Global Screening Array-24 Kit (Illumina, San Diego, CA, USA).

Data analysis will be done with the IBM SPSS Statistics program (version 29.0 Feb 2023).



Methods Description

Data Presentation

Epidemiological data will be presented in tables and according to frequency. The correlation evaluations of the SNPs will be carried out from the biostatistics databases.

The chi-square test will be performed for each SNP, in order to verify whether there is a relationship between the genotypes and responsiveness to conventional OA treatment and multiple test correction will be applied via Bonferroni.

Logistic regression analysis will be used to obtain the odds ratio for the relationship between SNPs and clinical outcomes for patients. Adjusted odds ratios and 95% confidence intervals for age, sex and BMI (covariates) will be used.

All tests will be two-tailed and with statistical significance for p-value less than 0.05

Results

Pilot Study

A pilot study was carried out with 5 participants in a cross-sectional evaluation with symptomatic chondral lesions and patients with osteoarthritis undergoing conservative treatments without clinical improvement. Spit samples were collected, quantified and DNA extracted, identifying 35 SNPs of interest. The other SNPs will be identified by the imputation method from the array.

Final Considerations

The present protocol was feasible to execute, and a large clinical trial will be performed. Genetic markers will allow personalized treatment and they have become a major topic of interest.

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References

1. Casalone, Elisabetta, Ioanna Tachmazidou, Eleni Zengini, Konstantinos Hatzikotoulas, Sophie Hackinger, Daniel Suveges, Julia Steinberg, et al. 2018. A Novel Variant in GLIS3 Is Associated with Osteoarthritis." *Annals of the Rheumatic Diseases* 77 (4). England: 620–23. doi:10.1136/annrheumdis-2017-211848.
2. Dai, Meilu, Baiyan Sui, Yang Xue, Xin Liu, and Jiao Sun. 2018. Cartilage Repair in Degenerative Osteoarthritis Mediated by Squid Type II Collagen via Immunomodulating Activation of M2 Macrophages, Inhibiting Apoptosis and Hypertrophy of Chondrocytes." *Biomaterials* 180. Elsevier Ltd: 91–103. doi:10.1016/ j.biomaterials.2018.07.011.
3. Diab, Safia M, Howyda M Kamal, Amira I Mansour, Rasha M Fawzy and Basma S Azab. 2017. Clinical Significance of Matrilin-3 Gene Polymorphism in Egyptian Patients with Primary Knee Osteoarthritis." *European Journal of Rheumatology* 4 (3). Turkey: 200–204. doi:10.5152/eurjrheum.2016.16107.
4. Farr, Jack, and Andreas H. Gomoll. 2016. !2016 Barriers To Cartilage Restoration." *Journal of Clinical Orthopaedics and Trauma* 7 (3). Delhi Orthopedic Association: 183 – 86 . doi: 10 . 1016 /j.jcot.2016.05.001.
5. Flanigan, David C, Joshua D Harris, Thai Q Trinh, Robert A Siston,and Robert H Brophy. 2010. !Prevalence of Chondral Defects in Athletes" Knees: A Systematic Review." *Medicine and Science in Sports and Exercise*. doi:10.1249/MSS.0b013e3181d9eea0.
6. Gomoll, Andreas H, Henning Madry, Gunnar Knutsen, Niek van Dijk, Romain Seil, Mats Brittberg, and Elizaveta Kon. 2010. !The Subchondral Bone in Articular Cartilage Repair: Current Problems in the Surgical Management." *Knee Surgery, Sports Traumatology, Arthroscopy : Official Journal of the ESSKA* 18 (4): 434–47. doi:10.1007/s00167-010-1072-x.
7. Liu, Youfang, Michelle S Yau, Laura M Yerges-Armstrong, David J Duggan, Jordan B Renner, Marc C Hochberg, Braxton D Mitchell, Rebecca D Jackson, and Joanne M Jordan. 2017. !Genetic Determinants of Radiographic Knee Osteoarthritis in African Americans." *The Journal of Rheumatology* 44 (11). Canada: 1652–58. doi:10.3899/jrheum.161488.
8. Meulenbelt, Ingrid, Josine L Min, Steffan Bos, Naghmeh Riyazi, Jeanine J Houwing-Duistermaat, Henk-Jan van der Wijk, Herman M Kroon, et al. 2008. Identification of DIO2 as a New Susceptibility Locus for Symptomatic Osteoarthritis." *Human Molecular Genetics* 17 (12). England: 1867–75. doi:10.1093/hmg/ddn082.
9. Perera, J R, P D Gikas, and G Bentley. 2012. !The Present State of Treatments for Articular Cartilage Defects in the Knee." *Annals of the Royal College of Surgeons of England* 94 (6): 381–87. doi:10.1308/003588412X13171221592573.
10. Samuelson, Eric M., and David E. Brown. 2012. !Cost-Effectiveness Analysis of Autologous Chondrocyte Implantation." *The American Journal of Sports Medicine* 4 0 (6) : 1 2 5 2 – 5 8 . doi:10.1177/0363546512441586.
11. Shen, Jie, and Di Chen. 2014. !Recent Progress in Osteoarthritis Research." *The Journal of the American Academy of Orthopaedic Surgeons* 22 (7). NIH Public Access: 467–68. doi:10.5435/ JAAOS-22-07-467.
12. Showery, James E., Nicholas A. Kusnezov, John C. Dunn, Julia O. Bader, Philip J. Belmont, and Brian R. Waterman. 2016. !The Rising Incidence of Degenerative and Posttraumatic Osteoarthritis of the Knee in the United States Military." *The Journal of Arthroplasty* 31 (10): 2108–14. doi:10.1016/j.arth.2016.03.026.
13. Valdes, Ana M, Deborah J Hart, Karen A Jones, Gabriela Surdulescu, Peter Swarbrick, David V Doyle, Alan J Schafer, and Tim D Spector. 2004. !Association Study of Candidate Genes for the Prevalence and Progression of Knee Osteoarthritis." *Arthritis and Rheumatism* 50 (8). United States: 2497–2507. doi:10.1002/art.20443.
14. Wang, Ting, Yuting Liang, Hong Li, Haibo Li, Quanze He, Ying Xue, Cong Shen, et al. 2016. !Single Nucleotide Polymorphisms and Osteoarthritis: An Overview and a Meta-Analysis." *Medicine* 95 (7). United States: e2811. doi:10.1097/MD.0000000000002811.
15. Zhang, Li, Limin Zhang, Haiqin Zhang, Wenjun Wang, and You Zhao. 2018. Association between SMAD3 Gene Rs12901499 Polymorphism and Knee Osteoarthritis in a Chinese Population." *Journal of Clinical Laboratory Analysis* 32 (5). United States: e22383. doi:10.1002/jcla.22383.