Sex Differences in Retinal Vascular Properties

With a focus on diabetes

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Project Goals:

- Explore differences of IDPs of the retina between males and females
- Study the association of IDPs with diabetes and other risk factors

About the Disease Diabetes

2 types :

Type I

- No production of insulin because of no ß cells in the pancreas (autoimmune disease).
- Multifactorial but with great genetic prevalence.
- Detectable in children and adolescents.

Type II

- Production of insulin that cannot be used, due to depletion of pancreatic ß cells.
- Due to bad lifestyle (malnutrition,

sedentarity, overweightness...)

- Detectable in adults (average = 45 years old)

Associated Diseases



Factors That Increase Diabetes Risk



Weight

Being overweight or

obese



Fat Distribution

Storage of fat in the abdomen, rather than hips & thighs



Age Risk increases with age



Inactivity Risk increases with increasing inactivity



Family History A parent or sibling having type 2 diabetes



Blood Lipid Levels

Low levels of "good" cholesterol High levels of triglycerides

https://www.mayoclinic.org/liseases-conditions/type-2-diabetes/symptoms-causes/syc-20351193

Diabetes in Men vs Women

Metabolic differences influence diabetes risk and the risk of vascular complications.

- Prevalence
- Proportion of vascular risk factors



https://link.springer.com/article/10.1007/s00125-019-05040-3 https://www.medrxiv.org/sontent/10.1101/2023.07.07.23 92368v1.full-text

Fundus Screening



Inexpensive, accessible, and timely

Could become an additional or alternative screening method for diabetes

https://onlinelibrary.wile.com/doi/epdf/10.1111/j.1365-2796.2010.02229.x https://www.medicinenet.com/what is the purpose of fundus photography/article.htm

Can be used to improve patient outcomes

- o Early and accurate diagnosis
- o Monitoring disease progression
- o Generate treatment plans



UK Biobank Data

Retina images from 81,859 subjects (from different assessment centers)

- 38,200 men
- 43,659 women

Used to extract vascular features from retinal images

- IDP = image derived phenotype
 - 17 IDPs measured
 - Separately for veins and arteries
 - Also for any vessel type, in general
 - Ratios also calculated

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Image Derived Retinal Phenotypes



Examples:

- Tortuosity
 - Vein, artery, and ratio
- Diameter
 - Veins and arteries
- Vascular density
 - Vein, artery, and total
- and many more...

Methods

Used various statistical methods:



1) Explorative statistics 2) Correlation analysis 3) Regression analysis

- Logistic regression
- Linear regression

Covariates Used

BMI

Body Mass Index

weight

height²

LDL

Low Density Lipoprotein "Bad cholesterol"

HDL

High density Lipoprotein "Good cholesterol"

Triglycerides

Source of ATP through the release of fatty acids

Initial Findings

- Larger proportion of men with diabetes than women
- Similar distribution of age at diagnosis for men and women
 - Differences in the 17 traits between men and women Differences in correlation between men and women

Age of diabetes by sex







Correlation differences between sex









Results

Differences in the IDPs between sex

-> <u>Does this difference have any impact with the</u> <u>correlation to diabetes and associated risk factors?</u>





https://www.medicine.mcgill.ca/epidemiology/joseph/courses/EPIB-621/interaction.pdf

Risk factor ~ IDP + sex + IDP*sex + confouding factors (age, assessment centers, spherical, and cylindrical power)

Associated risk factors studied:

- Triglycerides
- LDL
- HDL
- BMI

«Ordinary Least Square» model

Triglycerides



Triglycerides



Low Density Lipoprotein



Low Density Lipoprotein



High Density Lipoprotein

Confouding factors: age, assessment centers, spherical, and cylindrical power

-> Assessment center has a significant impact...







Diabetes ~ IDP + sex + IDP*sex + confouding factors (age, assessment centers, spherical, and cylindrical power)

-> Logistical model

Diabetes



Project Takeaways

- There are several differences in diabetes between men and women
 - Age of diagnosis
 - Number of cases
 - Significance of the 17 traits
- There are interaction between the IDPs and sex for most of the risk factors and diabetes

Project Challenges

• Statistical analysis

>>> Consideration of variables, binary vs continuous

- Obtaining results taking all variables into account (diabetes, sexes, IDPs, other covariates...) and create something consistent
- Significant differences between all assessment center in some cases
 - Samples with different sizes => Some of them are too small (background noise, less statistical power...)

Project Challenges

If we had more time...

- Look at confounding factors
 - i.e. smoking and alcohol



- Right, left, and both eyes separately
- Splitting the data into age categories