Retinal Vascular Features among South Indians

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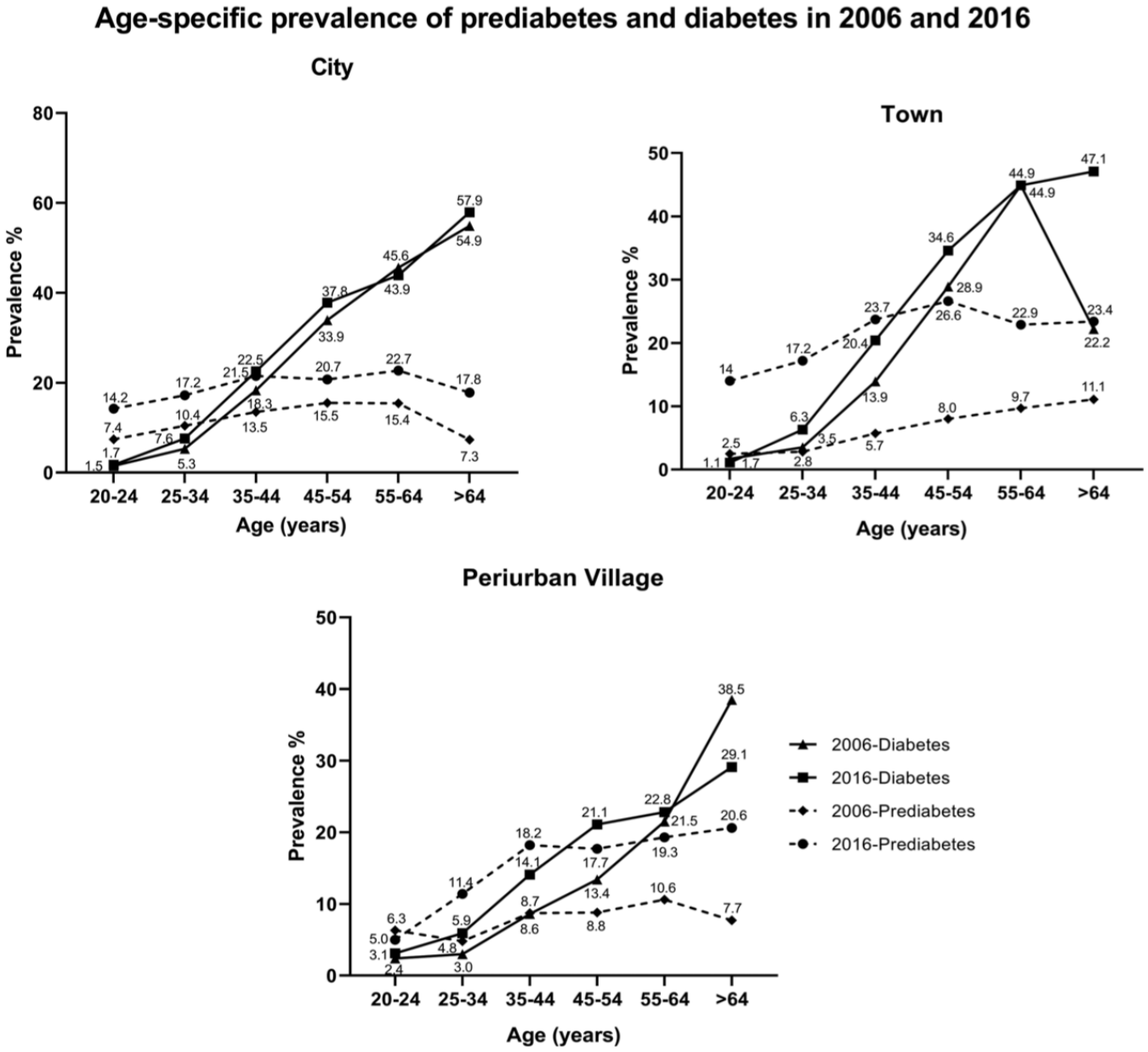
Outline

- Background
- Why explore retinal images as biomarkers?
- What are retinal vascular features?
- Retinal Data reduction.
- Methods
- Results
- Experiment
- Relationship between RVFs and Microvascular Complications: A Exploratory Analysis

Background

- India is one of the epicentre for diabetes in Asia.
- In Tamil Nadu, prevalence in increasing, especially in villages.



Secular TRends in DiabEtes in India (STRiDE–I): Change in Prevalence in 10 Years Among Urban and Rural Populations in Tamil Nadu. *Diabetes Care 2019;42:476–485 | https://doi.org/10.2337/dc18-1559*

Background

- Diabetes disproportionally increases risk of vascular complications.

Open access Research

BMJ Open Diabetes Research & Care

Real-world evidence of glycemic control among patients with type 2 diabetes mellitus in India: the TIGHT study

Surendra S Borgharkar,[1] Soma S Das[2]

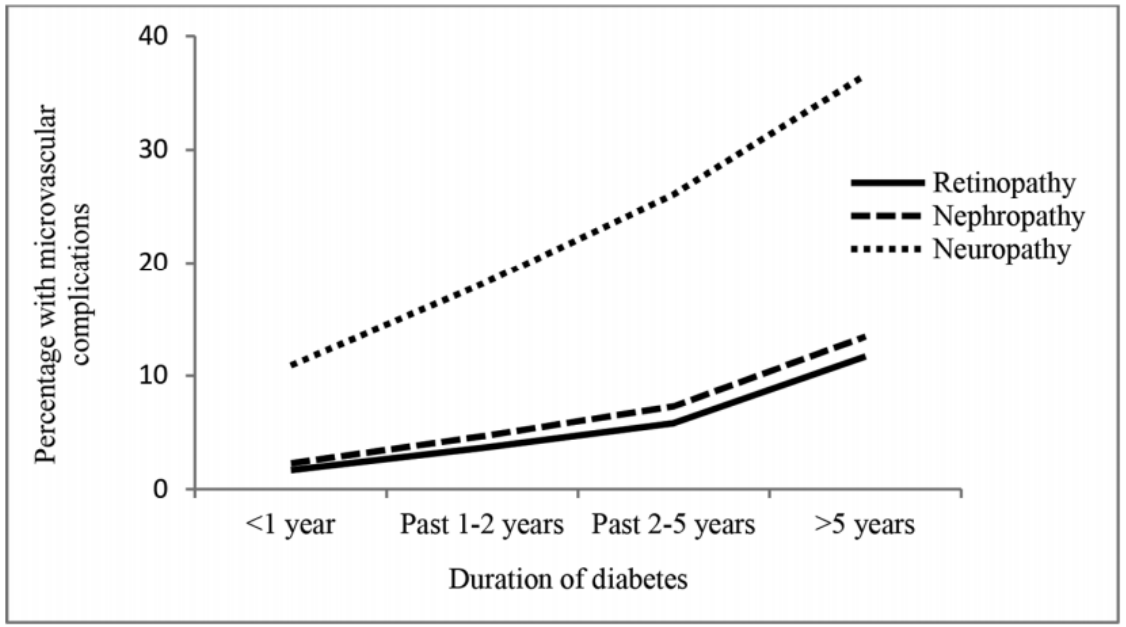


Figure 2 Duration of diabetes and various microvascular complications.

Why explore retina as potential biomarker?

- Non-invasive access to microvasculature (small blood vessels).
- Cost-effective and portable.
- Has to potential provide further information than DR severity.

Article | Published: 19 February 2018

Prediction Review Articles

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Insight

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Retinal Vascular Caliber as a Biomarker for Diabetes Microvascular Complications

M. Kamran Ikram, MD, PHD[1,2,3,4], Carol Y. Cheung, PHD[1,2,4], Mara Lorenzi, MD[5], Ronald Klein, MD, MPH[6], Teresa L.Z. Jones, MD[7], Tien Yin Wong, MD, PHD[1,2,4,8], for the NIH/JDRF Workshop on Retinal Biomarker for Diabetes Group*

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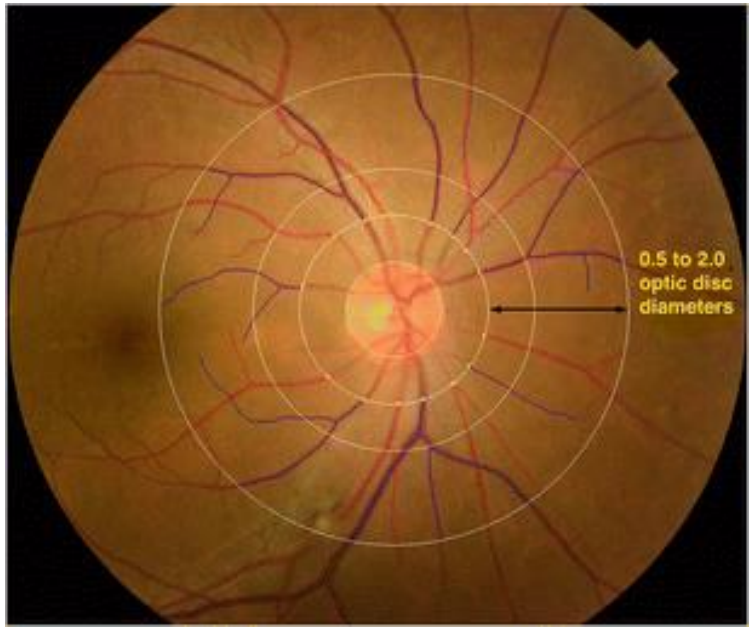
Diabetes Care 2013 Mar; 36(3): 750-759.

https://doi.org/10.2337/dc12-1554

Check for updates



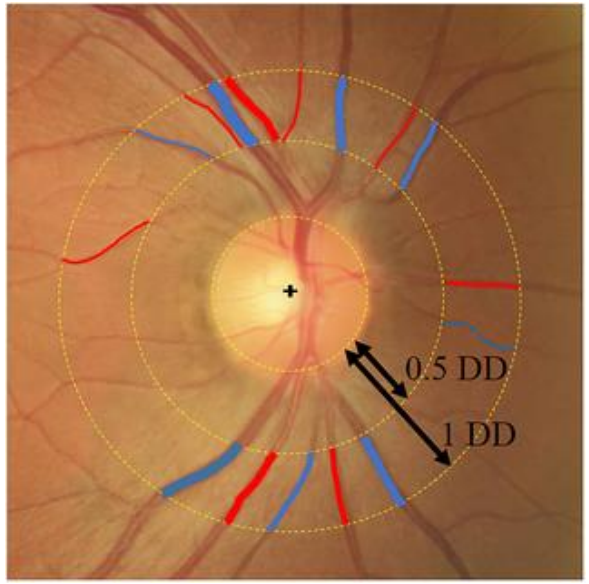
INSPIRED Project

- Utilise retinal fundus images to predict type 2 diabetic vascular complications among Scottish and South Indian participants.

What are retinal vascular features (RVFs)?

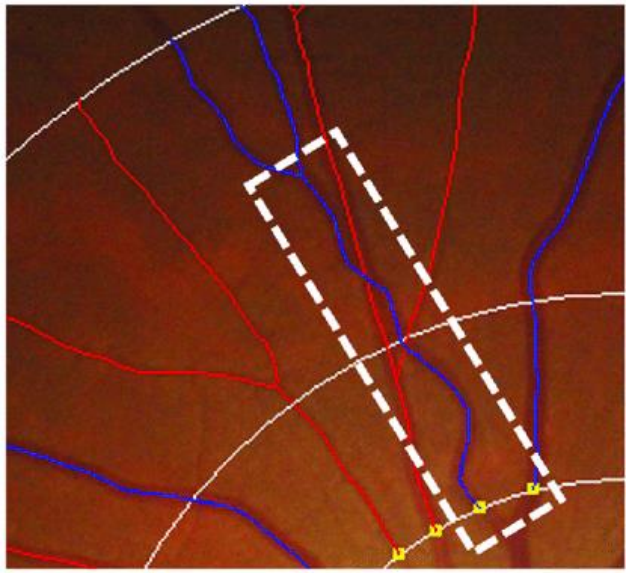
Vampire

Retinal vascular features (RVFs)?



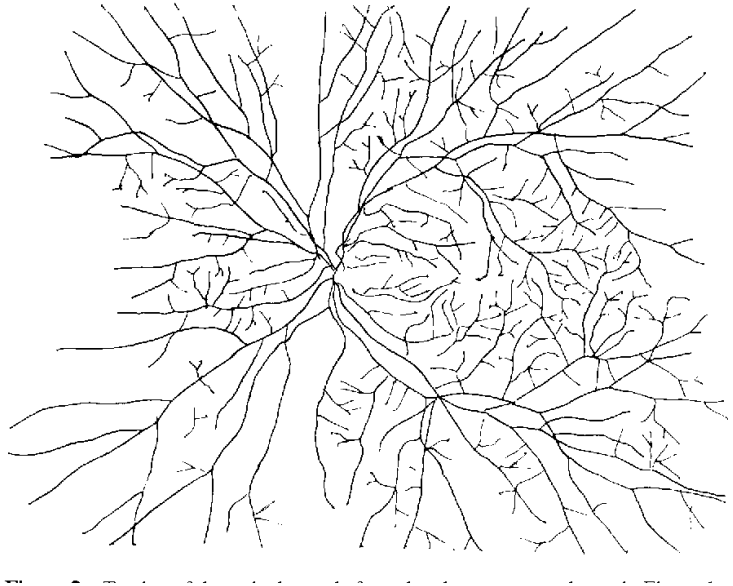
Retinal Vessel Calibre

Six largest vessel in Zone B



Retinal Vessel Tortuosity

Six largest vessel in Zone C



Retinal Vessel Fractal

Measured from vessels in Zone C

- These three are common retinal features measured from fundus image.
- Measurement technique may differ , but the measurement zone are same.

References:
1. DOI: 10.1371/journal.pone.0179663
2. DOI: 10.1371/journal.pone.0203868
3. DOI: 10.1146/annurev.bioeng.6.040803.140100

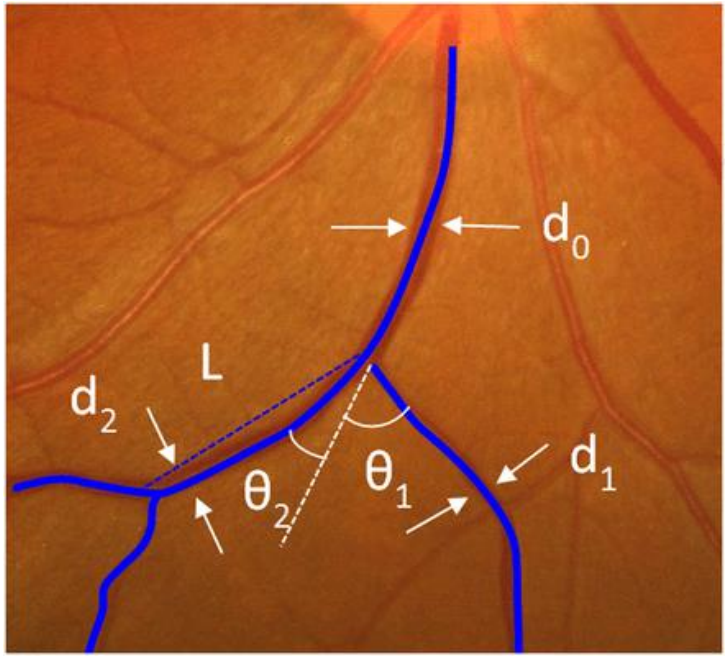
Additional RVFs

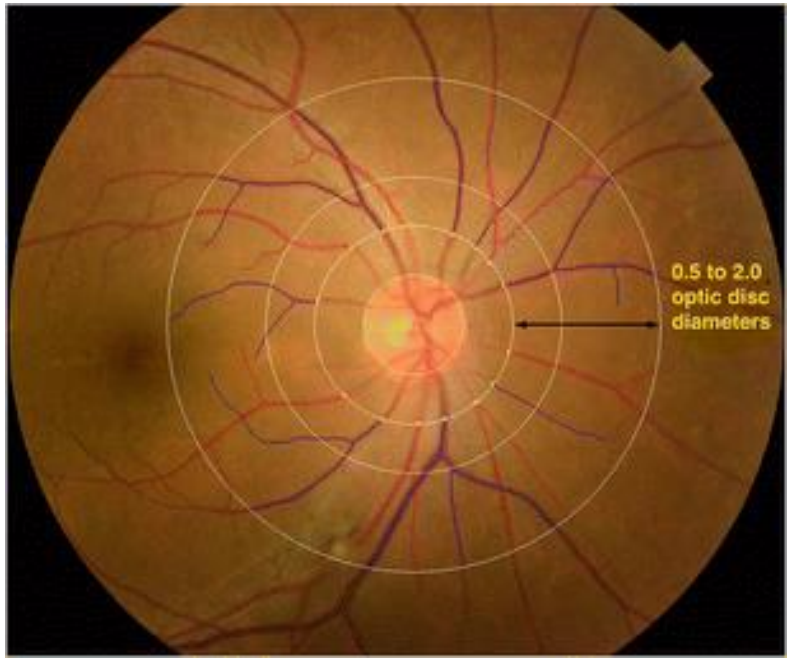
- Branching geometry and width gradient are calculated using *Spline* and *Hermite* methods.
- 32 measurements additional RVFs are measured.

≥150 variables to manageable number of variables

↓

Data Reduction Technique





RVFs	Definition
Branching Coefficient	Ratio of branching vessel widths to trunk vessel width $(d_1 + d_2)^2/d_0^2$
Asymmetry Factor	Ratio of the two branching vessel widths d_2^2/d_1^2.
Length-Diameter Ratio	Ratio of the length between two branching points to the trunk vessel width (L/d_0).
Width Gradient	Measured from main arteriolar path in each quadrant

Branching Geometry

Retinal images obtained from MDRF centre are optic disc centred images.

References:
1. https://doi.org/10.2337/dc12-1554

Retinal Data reduction

Methods

- Retinal images were obtained from participants who visited MDRF clinic for retinal screening.

- N=2,075 diabetic participants have retinal images measured using VAMPIRE software.

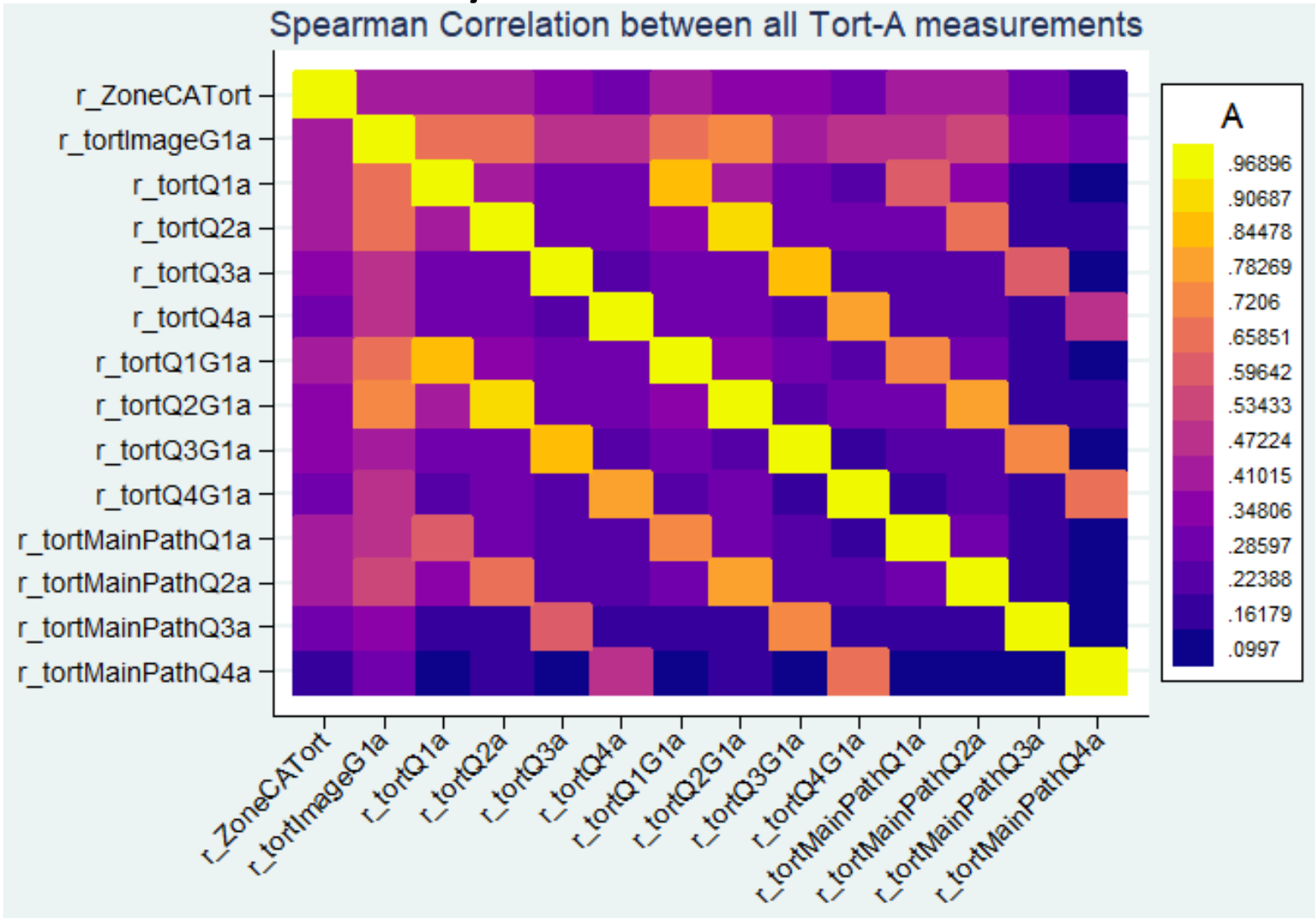
- PCA technique was used to perform data reduction as it reduces several correlated variables into several linearly uncorrelated variables.

- *Tortuosity*, *Branching Geometry* and *Width Gradient* measurements underwent data reduction technique using PCA.

- Tortuosity and width gradient measurements were log-transformed.
- Branching Geometry measurements were standardize.
- Fractal dimension measurements were retained on the basis of Pearson correlation coefficient.
- Decision to retain PC’s were based on Kaiser Index i.e. eigenvalue>1 and components which explained higher variance.

Results

Arteriolar Tortuosity



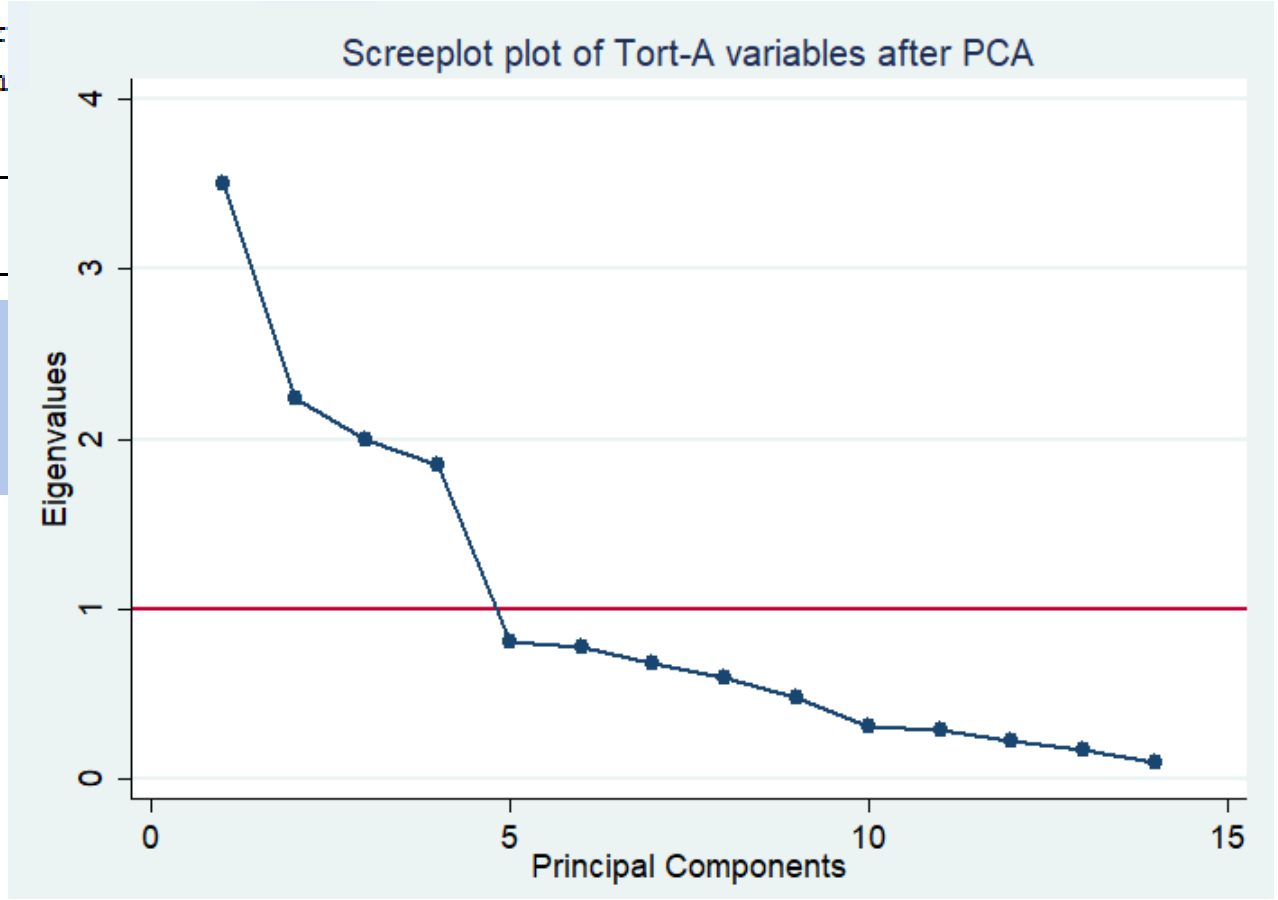
Moderate to high correlations observed between arteriolar tortuosity variables.

Arteriolar Tortuosity

```
Principal components/correlation                  Number of obs    =      1,051
                                                  Number of comp.  =         14
                                                  Tr
                                                  Rh
    Rotation: (unrotated = principal)
```

Component	Eigenvalue	Difference
Comp1	3.50337	1.26104
Comp2	2.24233	.251205
Comp3	1.99113	.149078
Comp4	1.84205	1.03865
Comp5	.8034	.0265315
Comp6	.776868	.097672

- 4 PC's show eigenvalue>1 and explain 68% variance, hence **retained.**



Variables Selected using PCA

Out of >150 VAMPIRE measurements obtained from MDRF participants, 22 were retained using PCA.

Original Dataset	PC's retained
Tortuosity • 28 arteriolar and venular measurements	4 PC's from arteriolar and venular each.
Width Gradient • 16 measurements	4 PC's retained
Branching Geometry • 16 measurements	4 PC's retained
Fractal Dimension • 3 arteriolar and venular measurements	1 arteriolar and venular measurement retained
Vessel Width • 2 Arteriolar and Venular Equivalent along with 2 Std. Deviation of A & V equivalent	All 4 measurements of arteriolar and venular equivalent along with std. deviation were retained.

Experiment

Relationship between retinal vascular features (RVFs) and microvascular complications among South Indian diabetic patients

Hypothesis: RVFs are associated with microvascular complications among diabetic patients.

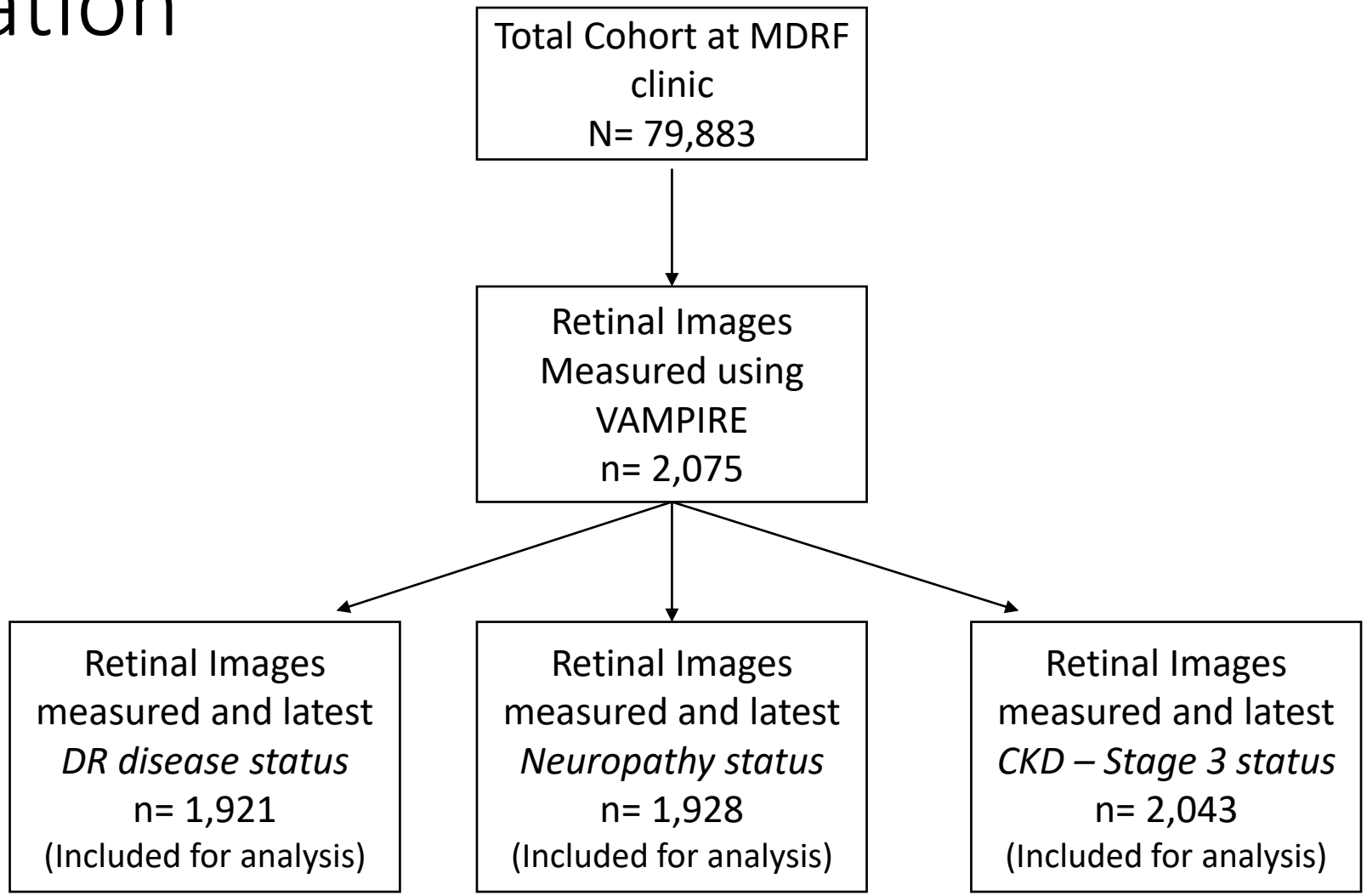
Methods

- Participants were recruited from diabetic specialist clinic in Chennai, India (MDRF).

- 2,075 participants who had retinal images measured using VAMPIRE software were included in this study.

- Participants disease status at latest visit was considered in events when participants visited to clinic more than once.

Study Population



Outcome Definition & Study Characteristics

	Microvascular Outcomes			
	Diabetic Retinopathy (DR)		**Chronic Kidney Disease (CKD)**	**Neuropathy (DPN)**
Definition	*Any DR*	*Proliferative DR*	*Stage 3 CKD*	
	Mild non-proliferative DR + Proliferative DR	Proliferative DR	eGFR≤60 mL/min/1.72m^2	Great Toe Test score more than 20

- Study Design: Cross-sectional
- Statistical Method: Logistic regression

Results

Relationship between Any Diabetic Retinopathy and Retinal Vascular Features *Number of participants with DR: 851 (44.30%)*				
RVFs	**Base Model**		**Full Model**	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Fractal Dimension-V $	0.88 (0.81 – 0.97)	0.01**	0.89 (0.81 – 0.99)	0.031*
Arteriolar Tortuosity PC1	1.11 (1.03 – 1.19)	0.006**	1.08 (1.00 – 1.17)	0.04*
Branching Geometry PC1	1.08 (1.01 – 1.16)	0.02*	1.09 (1.00 - 1.17)	0.031*
Relationship between Proliferative Diabetic Retinopathy and Retinal Vascular Features *Number of participants with PDR: 27 (1.41%)*				
Width Gradient PC1	0.68 (0.49 – 0.94)	0.02*	0.64 (0.44 – 0..93)	0.02*
Relationship between Chronic Kidney Disease and Retinal Vascular Features *Number of participants with CKD – Stage 3 : 126 (6.17%)*				
Vessel Width-A $	0.76 (0.62 - .092)	0.007**	0.73 (0.58 – 0.92)	0.008**
Fractal Dimension-A $	0.75 (0.63 – 0.89)	0.001***	0.74 (0.61 – 0.90)	0.004**
Branching Geometry PC2	0.83 (0.71 – 0.94)	0.006**	0.81 (0.69 – 0.94)	0.009**

Base Model : Adjusted for age and gender
Full Model : Adjusted for age, gender, HbA1c, sbp, smoke

*p≤0.05; **p≤0.01; ***p≤0.001
$: Standardize

Conclusion

- This study suggest relationship between RVFs and DR, and CKD – Stage 3.
- No relationship was detected between RVFs and diabetic neuropathy.
- Strength of the study, assessment conducted among large homogenous population.
- To my knowledge first study conducted among South Indian diabetic participants.
- Limitation of the study, cross-sectional nature the study.

Further steps

- Explore relationship between any microvascular complications and retinal vascular features among MDRF participants.

- Relationship between retinal vascular features and microvascular outcomes among type 2 diabetic patients: A GoDARTS study (Paper in Progress)

- Replicate these findings in GoDARTS population; but there are *challenges*:

1. Study Design: Prospective data points in GoDARTS after the date of image.
2. Centering Technique of retinal images, optic disk centered images in MDRF participants.

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GoDARTS
GENETICS OF DIABETES AUDIT AND RESEARCH TAYSIDE AND SCOTLAND

Vampire

MADRAS DIABETES RESEARCH FOUNDATION

INSPIRED
INdia-Scotland Partnership for pRecision mEdicine in Diabetes

NIHR | National Institute for Health Research

a BIG Thank You

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