AGE Reader

Non-invasive assessment of cardiovascular risk
Introduction

- Cardiovascular risk
- Measuring CV risk
- AGE Reader
- Clinical validation
Cardiovascular risk

- 70% of diabetics will die of CV event
- 5 out of 7 drugs (type 2 diabetic)
- Events are costly
- Difficult to assess
Measuring CV risk

Now in the clinic:

- Risk scores (UKPDS, SCORE, Framingham)
- Intima-media thickness
- Coronary calcification (CT scan)

- The AGE Reader gives
  - quickly and non-invasively
  - reliable extra information to help the physician to improve therapy
AGEs

- Advanced Glycation Endproducts
  - Glycated proteins

- AGE values rise in everyone when getting older.
  - But, much quicker in diabetes

- AGEs play a central role in the development of diabetes and cardiovascular risk.
AGEs

- AGE formation
AGEs

- AGEs causes major damage to tissue and cells
  - Irreversible malfunctioning proteins
  - Extreme long ½ life (many years)
  - In particular in diabetic patients
AGE Reader
AGE Reader

- Measurement report

Measurement report

Number: 01
Name: Raymon
Gender: Male
Age: 24

Measurement Results

AF 1.3
Measurement setting: Triple Measurement
Measured on: 26-2-2010 10:48

Healthy subjects
(Based on data from H. Koetsier et al., Diabetes Technol Ther, 2010)

AGEs
DiagnOptics AGE Reader is a medical device to estimate cardiovascular risk. The AGE Reader non-invasively assesses the accumulation of advanced glycation endproducts (AGEs) in the skin using fluorescence of ultraviolet light. AGEs play a pivotal role in the development of chronic complications of diabetes and other common conditions. The amount of AGEs in tissues serves as an important risk predictor of such complications.
Breakthrough publication

- Two important conclusions:
  - AGE measurement is best single predictor of (CV) mortality (after age)
  - When compared with whole risk engine:
    - independent
    - 27% re-classification
Additive predictive value skin AF on top of UKPDS risk score in type 2 diabetes (n=967)

Group 1. Both AF and UKPDS score < median
Group 2. AF > median and UKPDS score < median
Group 3. AF < median and UKPDS > median
Group 4. Both AF and UKPDS score > median

Event-free survival
(mortality + CV-morbidity)

Lutgers, Diabetol 2009
News Release

FOR IMMEDIATE RELEASE

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New Tool Can Help Predict Diabetes Complications

Other Studies This Month: Coffee Helps Prevent Diabetes;
When You Get Diabetes (Middle v. Old Age) Matters

(Alexandria, VA) – A noninvasive tool that measures the skin’s autofluorescence could help doctors determine whether people with diabetes are beginning to develop serious complications, according to a study published in the November issue of Diabetes Care.

Researchers in the Netherlands found that illuminating a patient’s lower arm with a fluorescent tube accurately reflects vascular damage caused by the accumulation of advanced glycosylation end products (AGEs). AGEs are produced in the body when glucose links with protein. They play a role in damaging blood vessels, which can lead to complications, such as nerve damage.

Previous studies have shown that AGEs have fluorescent properties. This study confirmed that those properties could be measured by illuminating the skin, and that high levels of autofluorescence were associated with more severe diabetes complications, such as neuropathy, retinopathy and cardiovascular problems.

“With this tool, doctors could easily check people with diabetes in an outpatient clinic setting to see whether they may already be developing dangerous complications,” said lead researcher Dr. Helen Lutgers, of the University Medical Center in Groningen, the Netherlands. “The sooner complications are detected, the better the chance of preventing progression of damage.”

The technology used in this study is currently commercially available in Europe. Until FDA approval is obtained, its availability in the USA is restricted to experimental use only.

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Case Report 1

AGE Reader and CV risk in clinical practice
Case Report

Ideal doctor: “when do I need to intensify treatment?”

Risk often in ‘grey’ zone
Ideal doctor knows: guidelines tell me to weigh other risk factors, but …..

- Metabolic syndrome, CRP, homocysteine: only marginal additive (to UKPDS RE) improvement in prediction of CV events
- Micoralbuminuria, renal dysfunction, hsCRP: require repeated sampling because of variability, medication, intermittent disease etc.
- IMT or coronary calcification score not generally available, expensive, radiation exposure. Still > 4-fold increase coronary CT in US over last decade (NEJM 2009)
Consequences of current guidelines in daily clinical practice

- Clinicians aware of weaknesses of risk scores
- Use UKPDS RS requires all 10 items and risk score result to be available at moment of patient visit to make decisions. In practice not so easy …
- Therefore, risk engines not used at all in majority!

- Similar situation for use of additional RF
- Then: to be on the safe side, doctor decides to intensify treatment
Case Report 2

CV risk in clinical practice

+ AGE Reader measurement
Clinical practice

- AGE Reader in clinical practice

Additive info with AGE reader:

If AF = 3.6 → median life expectancy this patient 25/2.62 = 9.5 yr

If the same patient has an AF = 2.4, → Median life expectancy 14.4 yr
Extension to T1DM

- Chabroux et al. (2010):
- French study in Lyon region in T1DM
- Confirms associations between AGE reader levels and nephropathy and neuropathy complications
Added proof in T2DM:

- **AURORA study:**
- Cross-sectional study in 566 T2DM patients controlled in 5 Dutch hospitals: sicker, higher HbA1c, more comorbidity
- Relation SAF with complications similar to previous study in primary care, better controlled patients
- SAF adds again to UKPDS!

Noordzij, EASD 2011; subm. Diabetes care
Renal failure

- CV complications and mortality in renal failure:
- In dialysis patients: 2 new, Japanese and Dutch, cohorts. Now studies available in 3 different cohorts on predictive value in hemodialysis patients
- More importantly: association SAF with CV complications extends also to CKD 3 (GFR 30-60 ml/min) (McIntyre, RRID; CJASN 2011):

Therapeutic implications more important in this group!
Conclusion

We have shown that tissue AGE, measured as SAF, is independently associated with multiple traditional and nontraditional risk factors for CKD progression and CVE in community-based participants with CKD stage 3. SAF measurement may therefore represent a clinically useful, noninvasive method for assessing renal and cardiovascular risk in participants with CKD. Planned follow-up for up to 10 years will evaluate this hypothesis in the RRID cohort.
USPs AGE Reader

- Clinically proven
- Non-invasive
- Reproducible
- No consumables
- Quick
- Easy to perform
Thank you for your attention