SERIOUS CLINICAL EVENTS IN HIV-POSITIVE PERSONS WITH CHRONIC KIDNEY DISEASE (CKD)

Disclosures

Nothing to disclose
Background

- CKD is becoming increasingly common in the ageing HIV-positive population with an estimated prevalence up to 30% in high risk populations\(^1\text{-}^3\)

- Risk factors (RF) for incident CKD amongst HIV-positive persons are well established\(^4\text{-}^9\) and include
  - Traditional renal RF (i.e. older age, hypertension & diabetes)
  - HIV related RF (i.e. immunosuppression & co-infections)
  - Antiretroviral treatment related RF (i.e. tenofovir disoproxil fumarate, indinavir, boosted atazanavir & lopinavir)

Background & Aims

• However, insights into the prognosis after CKD in persons with HIV is limited and requires a large dataset with substantial follow-up time.

• Aim to determine the prognosis and incidence of serious clinical events (SCE) after a diagnosis of CKD in persons with HIV and the role of modifiable risk factors.
Methods I

- D:A:D study participants under follow-up after 2004 (baseline for creatinine collection) with data on estimated glomerular filtration rate (eGFR) were included

- Incident CKD defined as:
  - Confirmed, > 3 months apart, eGFR ≤ 60 mL/min/1.73m² or
  - 25% eGFR decrease when baseline eGFR ≤ 60 mL/min/1.73m²

- SCE, were all centrally validated, included:
  - Cardiovascular disease (CVD)
    - myocardial infarction, stroke, invasive cardiovascular procedures
  - End stage renal disease (ESRD)
  - End stage liver disease (ESLD)
  - AIDS defining malignancies (ADM)
  - Non-AIDS defining malignancies (NADM)
  - Other AIDS events (excluding malignancies)
  - Death

- Recurrent SCE of the same type were excluded
Methods II

• Persons were followed from CKD to incident SCE, 6 months after last visit or Feb 1st 2016, whichever occurred first

• Kaplan Meier estimation calculated time to a SCE

• Poisson regression models considered associations between individual SCE and potential risk factors (time-updated when subjective to change over time)

• The population attributable risk fraction (PAF) was calculated for key identified risk factors (only those >5% presented)

• For perspectives, in a descriptive analysis, we followed participants from first eGFR to SCE and stratified follow-up time according to CKD status and compared crude rates of SCE between those with/without CKD
## Baseline Characteristics

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Rates of Incident SCE in HIV-Positive Persons With CKD

CKD
(2,467 persons*)
8,636 PYFU

Median 2.7 years (IQR 1.1-5.1)

SCE
595 persons (24.1%)
experienced 826 SCE events
IR 68.9/1,000 PYFU [95%CI 63.4-74.4]

*2,231 persons (90.4%) with eGFR ≤ 60 mL/min/1.73m² & 236 persons (9.6%) with 25% eGFR decline
SCE Incidence Rates & Distribution After CKD

Crude SCE IR/1000 PYFU after CKD (95%CI)

Any SCE: n = 595
Death: n = 313
NADM: n = 143
CVD: n = 137
Other AIDS: n = 123
ESRD: n = 72
ESLD: n = 19
ADM: n = 19
At 12 months 7.9% [6.9-9.0] were estimated to have any SCE & at 36 months 19.8% [18.0-21.0]
Underlying Cause of Death Following CKD (n=313)

- CVD: 20.1%
- Unknown: 10.9%
- Other AIDS: 8.0%
- ADM: 4.8%
- Liver: 6.1%
- Other Known: 16.6%
- Renal: 4.5%
- Bacterial Infection: 6.1%
- NADM: 23.0%
### Association Between Individual RFs & Main SCE After CKD

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<th>AdjustedIRR</th>
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*aIRR CVD (95%)*

*aIRR NADM(95%)*

*aIRR Other AIDS (95%)*

*aIRR Death (95%)*

Adjusted for age, gender, ethnicity, HIV acquisition, baseline date, smoking status, diabetes, hypertension, dyslipidaemia, eGFR, BMI, HBV and HCV status, *HIV control (poor CD4<350/VL>10000; good CD4>500/VL<400; Intermediate all other combinations), CD4 count, previous events (pre-baseline) and time-updated ESLD, ESRD, NADM, ADM other AIDS and CVD.
PAF (>5%) For Key Risk Factors For SCE After CKD

- BMI<18: 5.7% [2.7-7.8]
- eGFR<30: 13.7% [10.5-16.1]
- Dyslipidemia: 9.9% [-8.6-23.9]
  - CVD: 19.3% [9.7-25.3]
- Poor HIV control: 34.9% [27.7-40.2]
  - other AIDS: 13.5% [9.3-16.1]
- Diabetes: 11.8% [5.4-16.5]
  - NADM: 6.4% [2.1-9.2]
- Current smoking: 11.0% [1.4-17.9]
  - Other smoking: 8.1% [3.0-11.2]
  - 6.5% [0.0-10.2]
  - Current smoking: 6.1% [0.9-9.2]
Results in Perspective (I)
SCE in Persons With & Without CKD

Participants followed from first eGFR in D:A:D to SCE and follow-up and events stratified according to with/without CKD*

- **No CKD**
  - (34,116 persons*)
  - 272,424 PYFU
  - Median 8.8 years (IQR 5.8-10.8)
  - 6,300 persons (18.5%) with any SCE
  - IR 23.0/1,000 PYFU [22.4-23.6]

- **CKD**
  - (2,460 persons*)
  - 7,328 PYFU
  - Median 2.1 years (IQR 9.4-4.9)
  - 467 persons (18.9%) with any SCE
  - IR 63.7/1,000 PYFU [57.9-69.5]

*NOT the same population as previously; analysis has different inclusion and exclusion criterion for descriptive purposes only
Results in Perspective (II)
Crude SCE Incidence Rate Ratios in those With vs. Without CKD

ESRD
Death
CVD
NADM
Any SCE
ESLD
Other AIDS
ADM

Lower SCE rates with CKD
Higher SCE rates with CKD
Limitations

- Follow-up time after CKD was limited to median 2.7 years
- Possible effect modification by proteinuria could not be assessed as proteinuria data not collected systematically in D:A:D
- Risk of unmeasured confounding (e.g. use of NSAID)
- High proportion of participants with unknown ancestry due to national regulations
Conclusions I

- In an era where many HIV-positive persons require less monitoring due to effective antiretroviral treatment, those living with CKD have a high SCE burden with almost 1/5 developing SCE within 3 years, which require closer monitoring.

- Compared to persons without CKD, those living with CKD have substantially higher rates of organ dysfunction, NADM and non-malignant AIDS events.
Conclusions

- Our data further suggest modifiable risk factors including
  - Smoking for Death, CVD, Other AIDS & NADM
  - Dyslipidemia for Death & CVD
  - Poor HIV-control for Death & Other AIDS
  - Diabetes for Death & CVD
  - Low BMI and low eGFR for Death

play a central role for post-CKD morbidity and mortality and highlight the need of increased awareness, effective treatment and preventive measures for those living with CKD.
Acknowledgements

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**D:A:D coordinating office:** CI Hatleberg, L Ryom*, A Lind-Thomsen, RS Brandt, D Raben, C Matthews, A Bojesen, AL Grevsen, JD Lundgren*¢

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**External endpoint reviewer:** A Sjøl (CVD), P Meidahl (oncology), JS Iversen (nephrology)

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