**Kliiniline küsimus nr 13**

*Kliiniline küsimus tekst:* **Kas kõikidel kroonilise neeruhaigusega patsientidel sõltub komplikatsioonide teke:**

**- neerufunktsiooni muutusest vs mitte**

**- põhidiagnoosist vs mitte?**

Kriitilised tulemusnäitajad**:** **kroonilise neeruhaiguse ravi tulemuslikkus, komplikatsioonide teke, kroonilise neeruhaiguse progresseerumine, neeruasendusravi, südame-vereseoonkonna tüsistused, aneemia, sekundaarne hüperparatüreoidism, hospitaliseerimine, patsiendi elukvaliteet, ravikulu, elulemus, üldsuremuse vähenemine**

**Süstemaatilised ülevaated**

*Leiti 5 sobivat suuremahulist süstemaatilist ülevaadet. Autorid hindasid uuringute tugevuseks suurt osalejate hulka. Peamiseks nõrkuseks peeti lühikest järelkontrolli või jälgimisaega. Oluliseks hinnati komplikatsioonide tekkimise ennetamist, mis vähendab lõppstaadiumis neeruhaiguse teket ja suremust ning teisi võimalikke kaasuvaid tüsistusi. Samuti vähendab ravikulusid.*

**Viited**

| **Kokkuvõtte (abstract või kokkuvõtlikum info)** | **Viide kirjandusallikale** |
|---|---|
| Ühes retrospektiivses uuringus (Minutolo R. et. al; 2014) hinnati 30326 dialüüsivaba täiskasvanud patsienti, kellel oli krooniline neeruhaigus (staadiumites 1-5). Valim võeti 2002 ja 2003 aasta 700st erinevast Itaalia perearstikeskusest, kes kunagi ei olnud käinud nefroloogi konsultatsioonil. Kroonilise neeruhaiguse staadiumiteks loeti: 1 ja 2 (GFR 60 ml / min per 1,73 m2 ) ja oli ka albuminuuria või oli KNH diagnoositud rahvusvahelise koodi järgi, staadium 3a (GFR = 59-45), staadium 3b (GFR = 44-30), 4. staadium (GFR = 29-15) ja 5. staadium (GFR 15). Esmane tulemusnäitaja oli risk lõppstaadiumis neerupuudulikkusele (LSNP) (dialüüs või transplantatsioon) või üldisele suremusele.<br>**Tulemuste** järgi leiti, et KNH patsientidel oli risk LSNP ja suremusele suurem kroonilise neeruhaiguse staadiumites 3b-5. Lisaks leiti, et sõltumatud riskiyegurid LSNP ja suremusele (tabel 4) olid meessugu, diabeet ja koronaararterite haigus.<br>Leiti ka, et aneemia ja albuminuuria kahekordistavad LSNP ja suremuse riski vastavalt 56% ja 12% ulatuses. Ainult hüpertensioon, ilma teiste riskiteguriteta ei suurenda suremuse riski.<br><br>**Abstract**<br>**Background and objectives.** Rising prevalence of CKDrequires active involvement of general practitioners to limit ESRD and mortality risk. However, the outcomes of patients with CKD exclusively managed by general practitioners are ill defined.<br>Design, setting, participants, &measurements We prospectively evaluated 30,326 adult patientswith nondialysis CKD stages 1–5 who had never received consultation in tertiary nephrology care recruited from 700 general practitioner offices in Italy during 2002 and 2003. CKD stages were classified as stages 1 and 2 (GFR=60 ml/min per 1.73 m2 and either albuminuria or an International Classification of Diseases, Ninth Revision, Clinical<br>Modification code for kidney disease), stage 3a (GFR=59–45), stage 3b (GFR=44–30), stage 4 (GFR=29–15), and stage 5 (GFR,15). Primary outcome was the risk of ESRD (dialysis or transplantation) or all-cause death.<br>**Results** Overall 64% of patients were in stage 3a, and 4.5% of patients were in stages 3b–5. Patients with stages 1 and 2 were younger, were predominantly men, more frequently had diabetes, and had lower prevalence of previous cardiovascular disease than patients with stages 3a–5. Hypertension was frequent in all CKD stages (80%–94%), whereas there was a lower prevalence of dyslipidemia, albuminuria, and obesity associated with more advanced CKD. During the follow-up (median=7.2 years; interquartile range=4.7–7.7), 6592 patients died and 295 started ESRD. Compared with stages 1 | **Risk of ESRD and death in patients with CKD not referred to a nephrologist: a 7-year prospective study.**<br><br>**2014**<br><br>Minutolo R, Lapi F, Chiodini P.<br><br>**http://cjasn.asnjournals.org/content/9/9/1586.full.pdf+html** |

and 2 (reference), mortality risk (hazard ratio, 95% confidence interval)was higher in stages 3b–5 (1.66, 1.49–1.86, 2.75, 2.41–3.13 and 2.54, 2.01–3.22, respectively) but not stage 3a (1.11, 0.99–1.23). Similarly, ESRD risk (hazard ratio, 95% confidence interval) was not higher at stage 3a (1.44, 0.79–2.64) but was greater in stages 3b–5 (11.0, 6.3–19.5, 91.2, 53.2–156.2 and, 122.8, 67.9–222.0, respectively).
Among modifiable risk factors, anemia and albuminuria significantly predicted either outcome, whereas hypertension only predicted mortality.
**Conclusions** In patients with CKD not referred to nephrology, risks of ESRD and mortality were higher in those with CKD stages 3b–5.

**Table 4. Multivariable Cox model of determinants of ESRD and all-cause death**

| Variables | ESRD Hazard Ratio (95% Confidence Interval) | All-Cause Death Hazard Ratio (95% Confidence Interval) |
|---|---|---|
| Age (1 yr) | 0.96 (0.96 to 0.97)[a] | 1.10 (1.10 to 1.11)[a] |
| Women | 0.49 (0.39 to 0.63)[a] | 0.60 (0.57 to 0.63)[a] |
| Body mass index ≥30 kg/m$^2$ (yes versus no) | 0.71 (0.50 to 1.01) | 1.02 (0.94 to 1.11) |
| Hypertension (yes versus no) | 1.60 (0.93 to 2.76) | 1.11 (1.02 to 1.21)[a] |
| Diabetes mellitus (yes versus no) | 1.63 (1.26 to 2.11)[a] | 1.61 (1.52 to 1.70)[a] |
| Coronary artery disease (yes versus no) | 1.33 (1.03 to 1.71)[a] | 1.48 (1.41 to 1.56)[a] |
| Dyslipidemia (yes versus no) | 1.11 (0.86 to 1.44) | 0.67 (0.64 to 0.71)[a] |
| Anemia (yes versus no) | 2.08 (1.50 to 2.89)[a] | 1.56 (1.44 to 1.69)[a] |
| Albuminuria (yes versus no) | 2.11 (1.57 to 2.84)[a] | 1.12 (1.01 to 1.24)[a] |
| Use of RAS inhibitors (yes versus no) | 1.17 (0.89 to 1.53) | 1.02 (0.97 to 1.08) |
| **CKD stage** | | |
| 1 and 2 | Reference | Reference |
| 3a | 1.44 (0.79 to 2.64) | 1.11 (0.99 to 1.23) |
| 3b | 11.04 (6.26 to 19.48)[a] | 1.66 (1.49 to 1.86)[a] |
| 4 | 91.2 (53.2 to 156.2)[a] | 2.75 (2.41 to 3.13)[a] |
| 5 | 122.8 (67.9 to 222.0)[a] | 2.54 (2.01 to 3.22)[a] |

Hazard ratios are adjusted for all variables included into the model. RAS, renin-angiotensin system.
[a]Significant hazard ratio.

**Albuminuuria ja madala glomerulaarfiltratsiooni kiiruse (EGFR) täpne mõju kardiovaskulaarsele suremusele, üldsuremusele ja neerude töö halvenemisele diabeetikutel on ebakindel**.
Süstemaatiline ülevaade ( Toyama, T. et.al;2013) viidi läbi andmebaasidest MEDLINE, EMBASE ja CINHAL alates1950 kuni 2010 aastani. Sobivaks peeti ja võeti hindamiseks 31 kohortuuringud diabeeti põdevate inimesetega (148 350 patsienti). Tulemuseks arvutati kohandatud suhteline risk (RR), albuminuuria ja madala eGFR risk kardiovaskulaarsele suremusele, üldsuremusele ja neerude näitajate muutustele (joonis 3). (Albuminuuria defineeriti vt tabel 2)

**Tulemused:** Kardiovaskulaarsele suremusele olid mikroalbuminuuria (RR 1,76, 95% CI 1,38-2,25) ja makroalbuminuuria (RR 2,96 95% CI 2,44-3,60) olulised riskitegurid võrreldes normoalbuminuriaga. Sama trendi võis näha mikroalbuminuuria (RR 1,60, 95% CI 1,42-1,81) ja makroalbuminuuria (RR 2,64, 95% CI 2,13-3,27) riskil üldsuremusele ja ka mikroalbuminuuria (RR 3,21, 95% CI 2,05-5,02) ja makroalbuminuuria (RR 11,63, 95% CI 5,68-23,83) riskil neeru näitajate halvenemisele. Suhteline seotud risk madala eGFRi ja albuminuuriaga olid peaaegu võrdsed tõstes iga riski määra.
**Järeldused:** kõrge albuminuuria ja madal eGFR on olulised riskitegurid diabeeti põdevatel inimestel. Albuminuuria ja madal eGFR võivad olla teineteisest sõltumatud.
**Kokkuvõte:** Kõrge albuminuuria ja madal eGFR on riskiteguriks kardiovaskulaarsele suremusele, üldsuremusele ja neerude kahjustusele diabeeti põdevatel (vt. joonis 3). Mikro- ja makroalbuminuuria olid olulised riskitegurid kõigile kolmele väljundile. Vähem tõendeid oli ainult madala eGFR mõjust kardiovaskulaarsele suremusele, üldsuremusele ja neerude kahjustusele .

**Abstract**
**Background:** Precise effects of albuminuria and low estimated glomerular filtration rate (eGFR) on cardiovascular mortality, all-cause mortality, and renal events in diabetic patients are uncertain. Materials and Methods: A systematic review was conducted of the literature through MEDLINE, EMBASE, and CINHAL from 1950 to December 2010. Cohort studies of diabetic patients providing adjusted relative risk (RR) of albuminuria and eGFR for risks of cardiovascular mortality, all-cause mortality, and renal events were selected. Two reviewers screened abstracts and full papers of each study using standardized protocol.
**Results:** We identified 31 studies fulfilling the criteria from 6546 abstracts. With regard to the risk of cardiovascular mortality, microalbuminuria (RR 1.76, 95%CI 1.38–2.25) and macroalbuminuria (RR 2.96 95%CI 2.44–3.60) were significant risk factors compared to normoalbuminuria. The same trends were seen in microalbuminuria (RR 1.60, 95%CI 1.42–1.81), and macroalbuminuria (RR 2.64, 95%CI 2.13–3.27) for the risk of all-cause mortality, and also in microalbuminuria (RR 3.21, 95%CI 2.05–5.02) and macroalbuminuria (RR 11.63, 95%CI 5.68–23.83) for the risk of renal events. The magnitudes of

**The Impacts of Albuminuria and Low eGFR on the Risk of Cardiovascular Death, All-Cause Mortality, and Renal Events in Diabetic Patients: Meta-Analysis**

**2013**

Toyama, T, Furuichi, K, Niniomya,T. et.al.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3797878/

relative risks associated with low eGFR along with albuminuria were almost equal to multiplying each risk rate of low eGFR and albuminuria. No significant factors were found by investigating potential sources of heterogeneity using subgroup analysis.
**Conclusions:** High albuminuria and low eGFR are relevant risk factors in diabetic patients. Albuminuria and low eGFR may be independent of each other. To evaluate the effects of low eGFR, intervention, or race, appropriately designed studies are needed.

**Table 2**

**Definitions of Albuminuria.**

| Measurement Method | Microalbuminuria | Macroalbuminuria | Any level of albuminuria |
|---|---|---|---|
| 24 hour urine collection | 30–300 mg/day or 20–200 μg/min | >300 mg/day or >200 μg/min | >30 mg/day or >20 μg/min |
| (proteinuria) | N/A | >0.3–0.5 g/day | N/A |
| Spot urine albumin creatinine ratio | 30–300 mg/g or 3.4–34 mg/mmol | >300 mg/g or >34 mg/mmol | >30 mg/g or >3.4 mg/mmol |
| (proteinuria) | N/A | >0.3–0.5 g/g | N/A |
| Spot urine albumin concentration | 3–30 mg/dl | >30 mg/dl | >3 mg/dl |
| (proteinuria) | N/A | >0.3–0.5 g/l | N/A |
| Spot urine dipstick | Specific microalbuminuria dipstick positive | N/A | N/A |

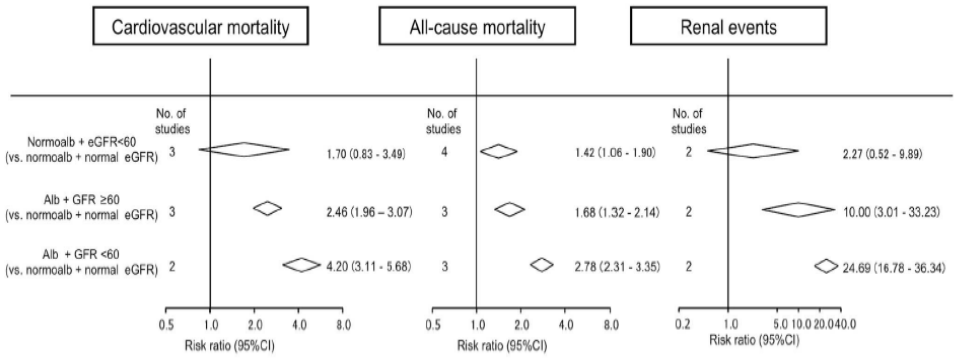


**Figure 3. Risk ratio for the association of low eGFR with the risk of each outcome according to the presence of albuminuria, compared with normal eGFR and normoalbuminuria.** Albuminuria was defined as any level of albuminuria or pooled estimate of microalbuminuria and macroalbuminuria. Abbreviations: normoalb, normoalbuminuria; alb, albuminuria.
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Neerupuudulikkus mängib kriitilist rolli südame isheemiatõve patogeneesis. Süstemaatilise ülevaate (Dan, K;2012) eesmärk oli uurida neerutalitlusehäirete levimust ja KNH mõju stabiilse stenokardiaga patsientidel kardiovaskulaarsete tüsistuste tekkeks (vasaku pärgarteri haiguse tekkeks (LMCAD)). Uuringusse kaasati 626 patsienti, kellel oli oluline pärgarteri stenoos. Krooniline neeruhaigus defineeriti eGFR <60 ml · min-1 · 1,73 m-2 ja/või esines proteinuuria. Analüüsid olid teostatud enne koronarograafiat.

**Tulemused:** Krooniline neeruhaigus oli seotud kardiovaskulaarse tüsistuse LMCADga (kohandatud riskisuhe, 1,74; 95% usaldusvahemik (UI)1,09-2,76, p = 0,01). 1-aastane järelkontroll näitas, et kummulatiivne esinemissagedus raskete kardiovaskulaarsete tüsistuste tekkeks (LMCAD) patsientidel, kelle eGFR oli <30 ml · min-1 · 1,73 m-2 oli suurem kui patsientidel, kelle eGFR oli ≥60 ml · min-1 · 1,73 m-2 (P = 0,03). Riskide suhe kardiovaskulaarsetele tüsistustele oli 9,54 (95% UI: 3,15-28,89, P <0,01) patsientedel, kellel esines LMCAD ( eGFR <30 ml · min-1 · 1,73 m-2) vs patsientidel ilma LMCAD (eGFR ≥60 ml · min-1 · 1,73 m-2).

**Krooniline neeruhaigus on riskiteguriks kardiovaskulaarsete tüsistuste (LMCAD) tekkeks stabiilse stenokardiaga patsientidel ja ennustab halba prognoosi. Seega on vaja tähelepanelik olla KNHga patsientide stabiilse stenokardia ravimisega.**

***Background:*** Renal insufficiency plays a critical role in the pathogenesis of ischemic heart disease. The aim of the present study was to investigate the prevalence of renal dysfunction and its impact on prognosis in patients with left main coronary artery disease (LMCAD) and stable angina pectoris.
***Methods and Results:*** A total of 626 consecutive patients with significant coronary artery stenosis were enrolled. Renal insufficiency was graded using estimated glomerular filtration rate (eGFR) before coronary angiography. Chronic kidney disease (CKD) was defined as eGFR <60 ml · min–1 · 1.73 m–2

**Impact of Chronic Kidney Disease on Left Main Coronary Artery Disease and Prognosis in Japanese Patients 2012**

Dan, K, MD; Miyoshi, T, MD;Ueeda, M. et.al.

https://www.jstage.jst.go.jp/article/circj/76/9/76_CJ-11-1455/_pdf

and/or proteinuria. Patients with LMCAD (n=95) had a significantly higher prevalence of CKD than those without LMCAD (P=0.02). Multiple logistic regression analysis showed that CKD was independently associated with LMCAD (adjusted odds ratio, 1.74; 95% confidence interval [CI]: 1.09–2.76, P=0.01). A 1-year follow-up of patients with LMCAD showed that the cumulative incidence of major adverse cardiovascular events among patients with eGFR <30 ml · min–1 · 1.73 m–2 was higher than that among patients with eGFR ≥60 ml · min–1 · 1.73 m–2 (P=0.03). The hazard ratio for a cardiovascular event was 9.54 (95% CI: 3.15–28.89, P<0.01) when comparing patients with LMCAD and eGFR <30 ml · min–1 · 1.73 m–2 vs. patients without LMCAD and eGFR ≥60 ml · min–1 · 1.73 m–2.

***Conclusions:*** Renal insufficiency is a risk factor for LMCAD and predicts poor prognosis in Japanese patients.

**Table 4. Effect of Renal Dysfunction on MACCE vs. Presence of LMCAD**

| eGFR (ml · min$^{-1}$ · 1.73 m$^{-2}$) | No. patients | MACCE (%) | HR (95%CI) | P value |
|---|---|---|---|---|
| **Non-LMCAD** | | | | |
| ≥60 | 123 | 7 | 1.00 | |
| ≥30, <60 | 111 | 21 | 2.39 (1.35–4.26) | <0.01 |
| <30 | 15 | 40 | 6.82 (3.21–14.52) | <0.01 |
| **LMCAD** | | | | |
| ≥60 | 24 | 17 | 2.25 (0.86–5.88) | NS |
| ≥30, <60 | 28 | 21 | 1.86 (0.70–4.93) | NS |
| <30 | 4 | 75 | 9.54 (3.15–28.89) | <0.01 |

This multivariate logistic analysis was adjusted for PCI and CABG.
HR, hazard ratio. Other abbreviations as in Tables 1–3.

**Neerufunktsiooni muutused on kõige tugevam südamepuudulikkuse prognoosija.** Neerufunktsioon ja neerufunktsiooni muutused annavad olulist kliinilist informatsiooni südamepuudulikkusega patsientidel. Nii neerufunktsiooni halvenemine kui äge neerupuudulikkus suurendavad suremuse riski ja südamepuudulikkuse süvenemist.
Süstemaatilises ülevaates (*Damman K*, et.al;2012) on vaadeldud ja võrreldud erinevaid neerufunktsiooni näitajaid ja markereid, mis näitavad ägeda- ja kroonilise südamepuudulikkuse prognoosi ja suremuse riski (tabelid 1 ja 2). Südamepuudulikkuse ja neerupuudulikkuse vastasmõjud ei ole staatilised vaid võivad olla dünaamilised, mõjutatud seisundi muutustest ja neurohormonaalsetest ja neerufunktsiooni muutustest, samuti mõjutab seda ravi. Seisundi muutused võivad areneda kiiresti ja võivad olla olulised või vastupidi aeglased ja ebaolulised.

Paremini, kui ainult kreatiniin võivad anda täpsemat teavet GFRi muutuste kohta markerid tsüstatiin-C ja uurea (tsüstatiini-C võib kasutada GFRi määramisel sarnaselt kreatiniini valemiga). Kliinilises praktikas on tsüstatiini-C valemit GFRi arvutamiseks vähe kasutatud ja seetõttu on väärtuste hindamisel vähe kogemusi. Kreatiniini baasil GFRi on arvutatud aastaid ning arstid teavad nende normväärtuseid. Igapäevaselt tsüstatiin-C määramine on ka oluliselt kallim võrreldes kreatiniini määramisega. Osad markerid võivad südamepuudulikkusega patsientidel prognoosida ägedaid neerufunktsiooni muutuseid veel enne kreatiniini muutust.
**Tabel 1.** annab ülevaate erinevate markerite seosest ägeda- ja kroonilise südamepuudulikkuse prognoosimisel.

**Abstract** Renal function is the most important predictor of clinical outcome in heart failure (HF). It is therefore essential to have accurate and reliable measurement of renal function and early specific markers of renal impairment in patients with HF. Several renal functional entities exist, including glomerular filtration (GFR), glomerular permeability, tubulointerstitial damage, and endocrine function. Different markers have been studied that can be used to determine changes and the effect of treatment in these entities. In the present review, we summarize current and novel markers that give an assessment of renal function and prognosis in the setting of acute and chronic HF.
**Conclusions.** The interaction between heart failure and renal impairment is not static, but comprises of dynamic changes in volume status, inflammatory response, neurohormonal activation and changes in renal function, by natural course, or in relation to therapy. These changes may be quick and substantial, but may also be slow and subtle. Finding the right marker to predict renal function in all of these situations may be impossible, but new markers are emerging that seem to perform better than serum creatinine alone. Some of these markers may give a good representation of GFR, such as cystatin C, BUN, while others give information on glomerular permeability (albuminuria) or tubulointerstitial damage (NAG, KIM-1, NGAL, and FABP). Importantly, the latter group (including IL-18) represents markers that may also predict acute changes in renal function, even before changes in creatinine occur. These markers are therefore suitable candidates as markers of treatment effect and as possible targets for therapy. New randomized clinical trials should, therefore, include measurement of these markers and possibly target these markers to preserve or even improve renal function in patients with HF.

**Current and novel renal biomarkers in heart failure**

**2012**

*Damman K1, Voors AA, Navis G*

**http://link.springer.com/article/10.1007%2Fs10741-011-9254-2**

**Table 1** Properties of different markers

| | Detection | "Validation" | Relation with prognosis | Pro's | Cons |
|---|---|---|---|---|---|
| *Glomerular filtration rate* | | | | | |
| Creatinine | Serum[a] | CHF | Strong evidence | Easy | Exponential relationship with GFR |
| | | AHF | | Cheap | Dependent on muscle mass |
| | | | | Interpretable | |
| (s)MDRD | Serum | CHF | Strong evidence | Valid | Formula (calculation) |
| | | Not in AHF | | Accurate | Less reliable in extremes of GFR |
| BUN | Serum | CHF | Emerging evidence | Easy | Interpretation difficult |
| | | AHF | | Cheap | |
| Cystatin C | Serum[a] | CHF | Evidence in AHF | Unbiased | Interpretation difficult |
| | | AHF | | Very reliable | Costs |
| *Glomerular permeability* | | | | | |
| Albuminuria | Urine | CHF | Strong evidence CHF | Easy obtainable | Low specificity |
| | | Not in AHF | | Cheap | |
| | | | | Additive to GFR | |
| *Tubulointerstitial damage* | | | | | |
| NAG | Urine | CHF | Emerging evidence CHF | Easy obtainable | Low specificity |
| | | Not in AHF | | Additive to GFR and UAE | Costs |
| | | | | Strong marker of AKI | |
| KIM-1 | Urine | CHF | Emerging evidence CHF | Easy obtainable | Costs |
| | | Not in AHF | | Additive to GFR and UAE | |
| | | | | Strong marker of AKI | |
| NGAL | Urine/ Serum | CHF | Emerging evidence CHF and AHF | Easy obtainable | Low specificity especially in serum and in CHF |
| | | AHF | | Additive to GFR and UAE | |
| | | | | Strong marker of AKI | |
| IL-18 | Urine/ Serum | CHF | Emerging evidence CHF | Easy obtainable | Also strongly increased in inflammation |
| | | Not in AHF | | Strong marker of AKI | |
| FABP-1 | Urine/ Serum | Not in CHF | None | Strong marker of AKI | Elevated in sepsis |
| | | Not in AHF | | | Also found in liver |

*AHF* acute heart failure, *AKI* acute kidney injury, *BUN* blood urea nitrogen, *CHF* chronic heart failure, *FABP* fatty acid binding protein, *GFR* glomerular filtration rate, *IL-18* Interleukin 18, *KIM-1* kidney injury molecule 1, *MDRD* modification of diet in renal disease (formula), *NAG N*-acetyl-beta-D-glucosaminidase, *NGAL* neutrophil gelatinase-associated lipocalin, *UAE* urinary albumin excretion

[a] Can be measured in urine, but then does not resemble GFR

**Table 2** Relationship between blood urea nitrogen and outcome in heart failure studies

| Study | Year | *N* | Setting | BUN (mg/dL) | Relative risk for mortality |
|---|---|---|---|---|---|
| Lee [25] | 2003 | 4031 | ADHF | 29 ± 19 | 1.49 (1.39–1.60) per 10 units increase |
| Aronson [19] | 2004 | 541 | ADHF | 34 ± 22 | 2.3 (1.3–4.1) for quartiles |
| Heywood [24] | 2005 | 680 | CHF | 29 ± 20 | BUN 30–50: 1.9, BUN >50: 2.2 |
| Shenkman [26] | 2007 | 257 | ADHF | 33 ± 22 | 3.6 (1.8–7.3) per log unit increase |
| Filippatos [21] | 2007 | 302 | ADHF | 31 ± 17 | 1.03 (1.00–1.05) per unit increase |
| Cauthen [20] | 2008 | 444 | CHF | 14 (6–22) | 1.04 (1.03–1.06) per unit increase |
| Klein [27] | 2008 | 949 | CHF | 25 (14–41) | 1.11 (1.07–1.15) per 5 units increase |
| Lin [22] | 2009 | 243 | CHF | 27 ± 17 | 1.24 (1.02–1.51) for BUN-to-creatinine ratio |
| Gotsman [23] | 2010 | 362 | ADHF | 23 (17–29) | 1.80 (1.30–2.49), per tertile BUN/creatinine |

*ADHF* Acute decompensated heart failure, *BUN* Blood urea nitrogen, *CHF* Chronic heart failure

Süstemaatilisse ülevaatesse (Turin TC, et. al;2012) kaasati 598 397 täiskasvanut, kellel oli vähemalt kahel ambulatoorsel külastusel mõõdetud eGFR (vähemalt 6 kuud) vähemalt 1 aasta jooksul. Retrospektiivne uuring toimus 1. maist 2002 kuni 31.märtsini 2008 ja jälgimisaeg kuni 31. märtsini 2009 ( jälgimisaja mediaan 3,5 aastat).

Vaadeldi neerufunktsiooni muutust kasutatades neerutalitluse muutuse määratlemiseks valemit: GFR kategooria arvutati [(viimane eGFR - esimene EGFR) / esimene eGFR × 100] ja väljendati protsentides (%).

Neerufunktsiooni muutused defineeriti järgmiselt: "teatud langus" (kroonilise neeruhaiguse kategooria EGFR langus ≥25% ); "ebakindel langus" (kroonilise neeruhaiguse kategooria EGFR langus <25%); "stabiilne" (kroonilise neeruhaiguse kategooria ei muutu); "ebakindel tõus (kroonilise neeruhaiguse kategooria EGFR tõus <25% ) ja" teatud tõus (kroonilise neeruhaiguse kategooria EGFR tõus ≥25%). Arvutati lõppstaadiumis neerupuudulikkuse (LSNP) kohandatud määr 1000 inimaastale.

**Tulemused:** Võrreldes stabiilse neerufunktsiooniga patsientide ja patsientide, kellel oli teatud GFRi langus tulemusi, (kohandatud ühismuutujatele ja esimesele eGFRi mõõtmisele) leiti, et teatud GFRi langusega patsientidel oli 5 korda suurem risk LSNPle (HR: 5,11; 95% CI: 4,56-5,71) . Ebakindla langusega GFR patsientidel oli 2 korda suurem risk LSNPle (HR 2,13; 95% CI: 1,84-2,47) võrrelduna stabiilse neerufunktsiooniga patsientidega.

Pärast eGFRi kohandamist ühismuutujatele, ei leitud seost suurenenud LSNP riskile ebakindla

**Short-term change in kidney function and risk of end-stage renal disease.**

**2012**

Turin TC, Coresh J, Tonelli M. et al.

http://ndt.oxfordjournals.org/content/27/10/3835.full.pdf+html

langusega eGFRi patsientidel.
**Riskisuhe LSNPle on seotud viimase eGFR mõõtmisega ja aja suhtega, HR 2,89 (95% CI: 2,35-3,55), 10.98 (95% CI: 8,69-13,87), 35.20 (95% CI: 27,95-44,32) ja 147,96 (116,92-187,23) vastavalt GFRi kategooriad 2, 3a, 3b ja 4 võrreldu na GFR 1 kategooriaga.** Riske LSNPle hinnati muutustega neerude funktsioonis ja võrreldi stabiilse neerufunktsiooniga.

Patsientidel, kellel tekkisid kategooriates "teatud muutused" neerude funktsioonis (nii langus kui tõus) olid vanemad, tõenäolisemalt naised ja neil oli suurem kaasuvate haiguste esinemissagedus võrreldes nendega, kellel oli stabiilne neerufunktsioon.
**Kokkuvõte:** Muutus eGFR kategooriates ≥25% langus (teatud langus) on seotud suurenenud LSNP riskiga, kuid tuleb arvestada ka patsiendi teisi näitajaid. Tulemustes leiti, et usaldusväärsemaks LSNP prognoosimiseks on vajalik määrata enam kui kahe seerumi kreatiniinisisaldust pikema perioodi jooksul kui 1 aasta.

**Abstract**
**BACKGROUND:** It is unclear what degree of change in the eGFR over a 1-year period indicates clinically significant progression, and whether this change adds additional information beyond that obtained by a single eGFR measure alone.
**METHODS:** We included 598 397 adults who had at least two outpatient eGFR measurements (at least 6 months apart) during 1-year accrual period in Alberta, Canada. Change in kidney function (using the first and last eGFR) was defined by change in kidney function category with confirmation based on percent (%) change in eGFR [(last eGFR - first eGFR)/first eGFR × 100]. The groups for change in kidney function were thus defined as: 'certain drop' (drop in CKD category with ≥25% decrease in the eGFR); 'uncertain drop' (drop in CKD category with <25% decrease in the eGFR); 'stable' (no change in CKD category); 'uncertain rise' (rise in CKD category with <25% rise in the eGFR) and 'certain rise' (rise in CKD category with ≥25% increase in the eGFR). Adjusted end-stage renal disease (ESRD) rates (per 1000 person-years) for each group of change in kidney function were calculated using Poisson regression. Adjusted risks of ESRD associated with change in kidney function, in reference to stable kidney function, were estimated.
**RESULTS:** Among the 598 397 participants, 74.8% (n = 447 570) had stable (no change in CKD category), 3.3% (n = 19 591) had a certain drop and 3.7% (n = 22 171) had a certain rise in kidney function. Participants who experienced a certain change in kidney function (both drop and rise) were older, more likely to be female, and had a higher prevalence of comorbidities, in comparison with those with stable kidney function. There were 1966 (0.3%) ESRD events over a median follow-up of 3.5 years. Compared with participants with stable kidney function, after adjustment for covariates, and the first eGFR measurement, those with certain drop had 5-fold increased risk of ESRD (HR: 5.11; 95% CI: 4.56-5.71), whereas those with an uncertain drop had 2-fold increased risk (HR: 2.13; 95% CI: 1.84-2.47). After adjustment for the eGFR and covariates at the last visit, neither a certain nor uncertain drop in the eGFR was associated with an increased ESRD risk. The ESRD risk associated with the last eGFR level, adjusted for the slope over time, were 2.89 (95% CI: 2.35-3.55), 10.98 (95% CI: 8.69-13.87), 35.20 (95% CI: 27.95-44.32) and 147.96 (116.92-187.23) for categories 2, 3a, 3b and 4, respectively, in reference to category 1.
**CONCLUSIONS:** A change in eGFR category accompanied by ≥25% decline (certain drop) is associated with increased ESRD risk. However, this elevated risk is captured by patient characteristics and eGFR at the last visit, suggesting that eGFR trajectories based on more than two serum creatinine measurements over a period longer than 1 year are required to determine ESRD risk and allow more reliable risk prediction.

**Table 1.** Baseline characteristics of study participants by 1-year change in kidney function

| | One-year change in kidney function, *n* (%) | | | | |
|---|---|---|---|---|---|
| | Certain drop, 19 591 (3.3) | Uncertain drop, 64 067 (10.7) | Stable, 447 570 (74.8) | Uncertain rise, 44 998 (7.5) | Certain rise, 22 171 (3.7) |
| Age, mean (SD), year | 63.3 (17.4) | 58.6 (15.1) | 54.6 (17.0) | 57.9 (14.8) | 59.9 (17.8) |
| Female gender (%) | 61.75 | 57.59 | 58.48 | 56.15 | 63.27 |
| Aboriginal (%) | 2.93 | 1.88 | 2.49 | 1.75 | 2.59 |
| Diabetes (%) | 23.39 | 15.09 | 13.05 | 13.78 | 16.27 |
| Hypertension (%) | 57.20 | 43.55 | 36.52 | 41.24 | 48.55 |
| Proteinuria (%) | | | | | |
| Normal | 41.97 | 54.42 | 57.15 | 55.97 | 48.25 |
| Mild | 9.86 | 6.35 | 5.89 | 6.23 | 8.69 |
| Heavy | 5.43 | 1.69 | 1.16 | 1.12 | 2.12 |
| Unmeasured | 42.74 | 37.54 | 35.80 | 36.68 | 40.95 |
| Kidney function at baseline (%) | | | | | |
| Category 1 | 36.14 | 67.10 | 45.03 | 0 | 0 |
| Category 2 | 40.84 | 23.34 | 45.74 | 71.47 | 44.81 |
| Category 3a | 13.96 | 7.58 | 5.96 | 21.30 | 32.11 |
| Category 3b | 7.22 | 1.78 | 2.48 | 6.09 | 16.61 |
| Category 4 | 1.85 | 0.20 | 0.79 | 1.14 | 6.47 |
| Cerebrovascular disease (%) | 8.05 | 4.40 | 3.48 | 3.84 | 6.30 |
| Peripheral vascular disease (%) | 6.40 | 2.93 | 2.16 | 2.56 | 4.04 |
| CHF (%) | 13.23 | 5.17 | 3.61 | 4.48 | 9.21 |
| COPD (%) | 23.02 | 17.75 | 16.42 | 17.05 | 20.83 |
| Cancer (%) | 10.90 | 6.92 | 6.01 | 6.31 | 8.93 |
| Dementia (%) | 5.12 | 2.31 | 1.81 | 2.26 | 4.54 |
| Myocardial infarction (%) | 8.62 | 4.38 | 3.29 | 3.95 | 5.99 |
| Mild liver disease (%) | 2.04 | 1.34 | 1.29 | 1.19 | 1.70 |
| Moderate liver disease (%) | 0.48 | 0.15 | 0.14 | 0.11 | 0.28 |
| Paralysis (%) | 1.31 | 0.63 | 0.60 | 0.49 | 0.87 |
| Peptic ulcer disease (%) | 4.38 | 2.83 | 2.70 | 2.77 | 3.83 |
| Rheumatic disease (%) | 3.61 | 2.42 | 2.09 | 2.16 | 2.93 |
| Socioeconomic status (%) | | | | | |
| Pensioner | 29.46 | 45.62 | 50.42 | 48.85 | 39.90 |
| Low | 10.52 | 12.55 | 12.12 | 13.07 | 10.51 |
| With subsidy | 4.68 | 3.28 | 3.73 | 3.10 | 4.62 |
| eGFR, mean (SD), mL/min/1.73 $m^2$ | | | | | |
| First measurement | 78.9 (24.1) | 84.8 (18.7) | 87.8 (21.4) | 76.4 (15.7) | 59.6 (17.8) |
| Last measurement | 51.4 (18.6) | 74.1 (17.0) | 87.8 (21.5) | 86.1 (17.4) | 84.1 (22.2) |

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease.
Data are in %, unless mean (SD). Totals do not always add to 100% because of rounding.

Figure 4. The unadjusted and adjusted (for covariates at the first measurement) risk of ESRD increased in a near exponential fashion with decline in kidney function defined by percent decrease in the eGFR. This association disappeared when adjustment for covariates were done at the last measurement of the eGFR.

**Table 2.**
ESRD rates, per 1000 person-years, by 1-year change in kidney function

| | One-year change in kidney function | | | | |
|---|---|---|---|---|---|
| | Certain drop | Uncertain drop | Stable | Uncertain rise | Certain rise |
| Events, *n* | 534 | 236 | 1061 | 62 | 73 |
| Patients, *n* | 19 591 | 64 067 | 447 570 | 44 998 | 22 171 |
| Adjusted for covariates at first measurement | | | | | |
| Rate (95% CI) | 0.77 (0.44–1.10) | 0.24 (0.13–0.36) | 0.18 (0.12–0.0.24) | 0.08 (0.02–0.14) | 0.05 (0.01–0.09) |
| Adjusted for covariates at last measurement | | | | | |
| Rate (95% CI) | 0.15 (0.10–0.21) | 0.11 (0.07–0.16) | 0.21 (0.15–0.26) | 0.29 (0.13–0.46) | 0.36 (0.16–0.55) |

CI, confidence interval.

Rates are adjusted for age, sex, diabetes, hypertension, socioeconomic status, kidney function, proteinuria and history of cancer, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, dementia, metastatic solid tumor, myocardial infarction, mild liver disease, moderate or severe liver disease, paralysis, peptic ulcer disease, peripheral vascular disease and rheumatic disease.

## Ravijuhendid

**Kokkuvõte ravijuhendites leiduvast**
**Antud kliinilisele küsimusele leidus ülevaateid kolmes sekretariaadi poolt AGREEga hinnatud ravijuhendis. Antud küsimuste soovituste tegemiseks on kasutatud väga kõrge kvaliteediga metaanalüüse.**

**KDIGO**
Tüsistuste esinemissagedus ja levik sõltub KNH staadiumist ja määratletakse valdavalt GFRi kategooriatetele ( vt. tabel 27).
Kõikidel ei teki kõiki tüsistusi, samuti tekivad tüsistused erineva kiirusega. Oluline on ühtselt teada võimalikke tüsistusi langeva eGFRi ja tõusva albuminuuria puhul.
KNH patsientidel on levinud tüsistuseks aneemia, kuid õige käsitlusega on võimalik hoida seda kontrolli all ( vt. aneemia ravijuhendit, http://www.njur.se/filer/behandlingsriktlinjer/riktlinjer_kdigo-anemia_gl.pdf).

**Soovitused**
**3.2.3: Teha kindlaks aneemia KNH inimestel määrates Hb kontsentratsioon (Not Graded):**
*** kui see on kliiniliselt näidustatud inimestele, kelle GFR on ≥60 ml / min / 1,73 m2 (GFR kategooriad G1-G2);**
***vähemalt kord aastas inimestel, kelle GFR on 30-59 ml / min / 1,73 m2 (GFR kategooriad G3A-G3B);**
***vähemalt kaks korda aastas inimestel, kelle GFR on <30 ml / min / 1,73 m2 (GFR kategooriad G4-G5).**

**4.1.1:Kõikidel KNH inimestel on suurenenud risk südame-veresoonkonna haigustele (1A).**

**4.1.2: Soovitame, et südame isheemiatõvega inimeste ravikäsitlus ei süvendaks kroonilist neeruhaigust. (1A)**

**4.3.1: Soovitame täiskasvanud KNH patsientidel regulaarselt jälgida perifeersete arterite haiguse ilminguid ja kaaluda tavalist teraapiasuunda. (1B)**

**4.3.2: Soovitame täiskasvanud KNHga ja diabeediga patsientidele regulaarset podiaatrilist hinnangut. (2 a)**

**3.2 COMPLICATIONS ASSOCIATED WITH LOSS OF KIDNEY FUNCTION**
People with CKD are prone to develop a variety of complications which reflect loss of endocrine or exocrine function **of**the kidneys. The incidence and prevalence of these complications increase with severity of CKD as defined predominantly by GFR categories (Table 27). It is beyond the scope of this guideline to describe each of the complications and the proposed treatment options for them in detail as guidance for these conditions can be found in other documents. However, for the purpose of completeness, the key complications and management recommendations for people with CKD are addressed in this section. In addition to these complications, we have described strategies to delay progression of CKD which are in part predicated on the identification and management of the clinical, metabolic, and hematologic complications. Note that not all people with CKD will have all of the complications and complications may not occur at the same rate or to the same degree in individuals with the same categories of GFR or albuminuria. Nonetheless knowledge of the common complications and treatment options is important in the care of CKD. Management of Complications Anemia in CKD. Anemia is an important complication of CKD because it contributes significantly to the heavy symptom burden of CKD. It has a major impact on the lives of people with CKD but it is potentially reversible with appropriate treatment. The guideline statements included here are those we consider to be the key considerations for people with non-dialysis CKD. Interested readers are referred to the KDIGO Clinical Practice Guideline for Anemia in for comprehensive guidance on this topic.

**Definition and identification of anemia in CKD**
**3.2.1: Diagnose anemia in adults and children ≥15 years**
**with CKD when the Hb concentration is o13.0 g/ dl (o130 g/l) in males ando12.0 g/dl (o120 g/l) in females. (Not Graded)**
**Evaluation of anemia in people with CKD**
**3.2.3: To identify anemia in people with CKD measure Hb concentration (Not Graded):**
**when clinically indicated in people with GFR**
**≥60 ml/min/1.73 m2 (GFR categories G1-G2);**
**at least annually in people with GFR 30-59 ml/ min/1.73 m2 (GFR categories G3a-G3b); at least twice per year in people with GFR o30 ml/min/1.73 m2 (GFR categories G4-G5).**

**4.1.1: We recommend that all people with CKD be considered at increased risk for cardiovascular disease. (1A)**

In those with an eGFR of 45-59 ml/min/1.73 m2, risk is increased by 43% and in those with eGFR below 15 ml/min/1.73 m2, risk is increased by 343%.58 Although people with GFR category G5 (GFRo15 ml/min/1.73 m2) are at the highest risk of a CVD event, there will be more events in people with GFR categories G3a-G3b (GFR 30–59 ml/min/1.73 m2) because of the much higher prevalence at these categories.420 These events occur at a younger age in people with CKD suggesting that CKD promotes CVD at an accelerated rate.421 The prognosis after an acute event is related to level of GFR with a significant rise

in mortality when eGFR falls below 45 ml/min/1.73 m2.[422–424]
The Chronic Kidney Disease Prognosis Consortium demonstrated that in general practice cohorts there was an increase in cardiovascular mortality when ACR is higher than 30 mg/g (3 mg/mmol).[4] Analysis of data from the Heart Outcomes Prevention Evaluation (HOPE) study demonstrated that any degree of albuminuria is a risk factor for cardiovascular events in individuals with or without diabetes.[428]

**4.1.2: We recommend that the level of care for ischemic heart disease offered to people with CKD should not be prejudiced by their CKD. (1A)**

**4.3.1: We recommend that adults with CKD be regularlyexamined for signs of peripheral arterial disease and be considered for usual approaches to therapy. (1B)**

**4.3.2: We suggest that adults with CKD and diabetes are offered regular podiatric assessment. (2A)**

**Table 31 | Peripheral arterial disease and CKD**

| Study | Population | PAD definition | Outcome of interest |
|---|---|---|---|
| O'Hare et al.[585] | NHANES age 40+ | ABI <0.9 | 24% prevalence in people with CKD and a CrCl of <60 ml/min (< 1 ml/s) versus 3.7% in those with normal kidney function |
| O'Hare et al.[587] | HERS study, postmenopausal women with known CHD | PAD event rates (amputation, revascularization, or lumbar sympathectomy) | Incident PAD event rates were 0.55%, 0.92%, and 2.73% per year with CrCl 60, 30-59, and 30 ml/min/1.73 $m^2$, respectively |
| O'Hare et al.[586] | Cardiovascular Health Study, adults age 65+ | Lower-extremity PAD procedure (bypass surgery, angioplasty, or amputation) | HR for PAD procedure 2.5 (95% CI 1.2-5.1) for highest quintile of cystatin C (≥1.28 mg/l) versus lowest (≤0.9 mg/l) |
| De Vinuesa et al.[582] | 102 adults in a CKD clinic, mean age 70 ± 11 years, GFR 15-60 ml/min/ 1.73 $m^2$ | ABI <0.9 | 17% signs and symptoms of PAD, which had passed unnoticed; 32% had ABI <0.9 (mean 0.64 ± 0.25) |
| Liew et al.[584] | 6-year follow up of 1027 subjects (ABI index recording and GFR measured within 90 d) | ABI <0.9 | 6-year mortality rate for CKD and PAD 45% versus 28% CKD alone, 26% PAD alone, and 18% for neither condition |
| Wattanakit et al.[588] | 6760 subjects, aged 45-84 years in the Multi-Ethnic Study of Atherosclerosis | ABI <0.9 | Albuminuria was associated with PAD in subjects with diabetes (odds ratio 1.90, 95% CI 1.19–3.04) but not in those without |
| Lash et al.[583] | 3612 subjects age 58.2 ± 11.0 years in the Chronic Renal Insufficiency Cohort study | ABI <0.9 | Overall, 16% prevalence of PAD in subjects with GFR<60 ml/min/1.73 $m^2$, increasing from 4% in those with GFR>60 to 22% in those with GFR<30 ml/min/1.73 $m^2$ |
| Bello et al.[581] | 920,985 subjects with GFR and proteinuria assessment, median follow-up 35 months (IQR 22-44) | Time to first hospitalization with PAD | 1891 of subjects (0.2%) hospitalized at least once for PVD, adjusted rates increased with lower GFR |

Abbreviations: ABI, ankle-brachial index; CHD, coronary heart disease; CI, confidence interval; CKD, chronic kidney disease; CrCl, creatinine clearance; d, day; GFR, glomerular filtration rate; HERS, Heart and Estrogen/Progestin Replacement Study; HR, hazard ratio; IQR, interquartile range; NHANES, National Health and Nutrition Examination Survey; PAD, peripheral arterial disease; PVD, peripheral vascular disease.

**Table 41 | Final grade for overall quality of evidence**

| Grade | Quality of evidence | Meaning |
|---|---|---|
| A | High | We are confident that the true effect lies close to that of the estimate of the effect. |
| B | Moderate | The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| C | Low | The true effect may be substantially different from the estimate of the effect. |
| D | Very low | The estimate of effect is very uncertain, and often will be far from the truth. |

**Table 42 | Balance of benefits and harm**

When there was evidence to determine the balance of medical benefits and harm of an intervention to a patient, conclusions were categorized as follows:

- For statistically significant benefit/harm, report as 'benefit [or harm] of drug X'.
- For non-statistically significant benefit/harm, report as 'possible benefit [or harm] of drug X'.
- In instances where studies are inconsistent, report as 'possible benefit [or harm] of drug X'.
- 'No difference' can only be reported if a study is not imprecise.
- 'Insufficient evidence' is reported if imprecision is a factor.

**NICE**

Ravijuhendis kasutatud üks kõrge kvaliteediga IPD meta-analüüs näitab, et on olemas suundumus, et eGFR suurem langus on seotud tõusva albuminuuriaga(ACR). Kelle eGFR on 15-29ml / min / 1,73 m2, ainult ACR on suurem kui 10 mg / g ennustab langust eGFR, kuigi kõik kategooriad ennustavad eGFR 30-59ml / min / 1,73 m2. Kelle eGFR on suurem kui 90 ml / min / 1,73 m2 on ebaselge, kas ACR lisab sellele ennustatavat väärtust.
Kaks kõrge kvaliteediga IPD meta-analüüsi näitab, et kõigil eGFR kategooriatel on trend LSKN (lõppstaadiumis krooniline neeruhaigus) sagenemisele süveneva proteinuuria (PCR) ja albuminuuria (ACR) korral. Kui kihistunud eGFR, ACR ennustab oluliselt suuremat risk LSKN eGFR 15-29, 30-44 ja 45-59ml / min / 1,73 m2, kuid trend väheneb suuremate eGFR-ide puhul.
LSNK prognoosi vahe ei ole selge üle või alla 65-aasta vanustel eGFR või ACR muutumisel, välja arvatud eGFR 15-29ml / min / 1,73 m2, kus suurenev ACR võib ennustada LSKN inimestele alla 65-aastane, kuid usaldusintervall on väga lai.
Teine IPD meta-analüüs näitas, et seos vähenenud eGFRi ja suurenenud risk neerufunktsiooni halvenemisele vähenes

vanuse suurenedes (üle 54-aastased), kuid see ei olnud nii ilmne ACR.
Puudub ühtne erinevus progresseerumise riskile, erinevatel eGFR kategooriatel või ACR, inimestestel:
o koos või ilma diabeetita
o või ilma hüpertensioonita.

**Üldsuremus**

Üks kõrge kvaliteediga IPD meta-analüüs ei viita koos PCR tasemega ja sagedusega üldsuremusele. Kasvav ACR ennustab suurenenud üldsuremust, kuid eristamine ACR kategooriates on ebaselge, kuna usaldusvahemikud kattuvad. ACR suurem kui 30 mg / g ennustab oluliselt suurenenud üldsuremust kõikides eGFR kategooriates.
Ei ole selget vahet riski üldsuremusele igal eGFR või ACR kategoorias, kas sõltub vanusest (alla või üle 65-aastased) või kaasuvast diabeedist. Teine IPD meta-analüüs näitas, et seos vähenenud eGFR ja suurenenud suremuse risk vähenes vanuse suurenedes (üle 54-aastased), kuid see oli koos ACRiga.
Hüpertensioon näitas samasuguseid tulemusi ACR kategoorias 10-29mg / g, mis ennustab rohkem üldsuremuset hüpertensiooniga inimestel, kuigi usaldusvahemik on väga lai.

**Kardiovaskulaarne suremus**

Üks kõrge kvaliteediga IPD meta-analüüs näitas, et kui ACR tase on suurem kui 300 mg / g ennustab see rohkem kardiovaskulaarset suremust kui ACR on 10-29 või 30-299mg / g.
Ei ole selge erinevus kardiovaskulaarse haigestumuse kohta kõigil eGFR staadiumitel või ACR kategoorias vanuserühmades (alla või üle 65-aastased) või kaasuva diabeedi või hüpertensiooni diagnoosiga inimestel.

**ÄNP**

Üks kõrge kvaliteediga IPD meta-analüüs näitas, et progresseeruv albuminuuria ennustab ÄNP ( äge neerupuudulikkus).

**Soovitused**

**Liigitada krooniline neeruhaigus kasutades kombinatsiooni GFR ja ACR kategooriad (nagu on kirjeldatud tabelis 27).**

**Pea meeles, et:**

**Suurenenud ACR on seotud suurenenud riskiga kõrvaltoimete tekkeks.**

**Langenud GFR on seotud suurenenud riskiga kõrvaltoimete tekkeks.**

**Suurenenud ACR ja langenud GFR kombinatsioonis tõstab kõrvaltoimete riski. Ärge juhinduge kroonilise neeruhaiguse diagnoosimisel ainult vanusest.**

**Kasutage isiku GFR ja ACR kategooriad (vt tabel 27), mis näitab nende kõrvaltoimete riski tulemusi (näiteks kroonilise neeruhaiguse progresseerumist, äge neerukahjustus, üldsuremust ja kardiovaskulaarset haigust) ja arutada seda koos nendega.**

## 6.1 The influence of GFR, age, gender, ethnicity and proteinuria on patient outcomes

### 6.1.1 Introduction

In 2002 the US National Kidney Foundation Kidney Disease Outcomes Quality Initiative published a classification of chronic kidney disease split into five stages defined by glomerular filtration rate (GFR). Although internationally accepted, a classification of CKD based solely on GFR category has been the subject of debate in the intervening years. In 2008 NICE clinical practice guideline CG73 recommended adjusting this classification to sub-divide stage 3 CKD into 3a (GFR 45-59 ml/min/1.73 $m^2$) and 3b (GFR 30-44 ml/min/1.73 $m^2$) on the basis of a clear difference in adverse outcomes associated with the 2 different GFR categories. NICE CG73 also recognised the importance of associated proteinuria, recommending the addition of a suffix p for those with significant proteinuria (defined as urinary albumin:creatinine ratio (ACR) >30 mg/mmol), to delineate people at increased risk of adverse outcome. Recent epidemiological studies have focussed on determining the influence of differing levels of proteinuria on outcomes in all categories of GFR. The purpose of this question was to review these new data to determine whether the definition and classification of chronic kidney disease should be further refined.

**6.1.2 Review question: For people with suspected CKD, what is the effect of proteinuria at any given eGFR on adverse outcomes?**

Update 2014

For full details see review protocol in Appendix C.

**Table 23: PICO characteristics of classification review question**

| | |
|---|---|
| **Population** | Adults (aged 18 and over) with suspected CKD |
| **Prognostic factor** | Proteinuria:<br>• ACR <3 mg/mmol (<30mg/g)<br>• ACR 3-29 mg/mmol (30-299mg/g)<br>• ACR >30 mg/mmol (>300mg/g)<br>(or equivalent PCR and reagent strip result |
| **Outcomes** | Critical<br>• CKD progression: change in eGFR<br>• CKD progression: occurrence of end stage kidney disease (ESRD or ESKD as reported by the study)All-cause mortality<br>• Cardiovascular mortality<br>• AKI<br>Important<br>• Cardiovascular events<br>• Hospitalisation |
| **Study design** | Prospective cohort studies, meta-analysis<br>(retrospective cohort studies if prospective studies not identified) |

### 6.1.3 Clinical evidence

Six individual patient data (IPD) meta-analyses were included in the review.[21,108,117,134,237,408] Evidence from these are summarised below in Table 25, and a narrative summary of results in the evidence statements. See also the study selection flow chart in Appendix D, forest plots in Appendix I and study evidence tables in Appendix G.

As these studies are all IPD meta-analysis, quality was assessed per-study using a customised methodology checklist for quality assessment of systematic reviews of prognostic studies adapted from Hayden 2006[138] rather than by using the GRADE profile. The study quality rating is given in the final column of Table 25. A narrative summary of results is provided in place of the GRADE summary of findings table.

The included IPD meta-analyses addressed the review question directly and covered all subgroups in the review protocol, therefore individual cohort studies were excluded from this review (Appendix J).

No evidence was identified reporting hospitalisation or cardiovascular events.

The IPD meta-analyses included study populations of people with CKD,[21] populations at high risk of chronic kidney disease,[117,408] those with and without diabetes[108] and those with and without hypertension[237]. Gansevoort et al.[117] also included data from general population cohorts, but data from high risk cohorts was presented separately in the analysis due to important baseline differences between the groups, and only the high risk data are included in this review. Hallan et al.[134] included general population, high risk and CKD cohorts. Although CKD cohorts were separated for analysis of mortality and ESRD, hazard ratios could not be calculated from the data presented. The overall data has therefore been presented as this also separates by eGFR and ACR categories. Although these three studies included populations that could be considered indirect to the review target population (both included data from general population cohorts as well as high risk and CKD cohorts), they were included as they addressed subgroups of interest and provided data on eGFR and proteinuria levels from which CKD status could be derived.

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References to the individual cohorts included in each of the meta-analyses are provided in the evidence tables in Appendix G.

All ACR and PCR data in this review are in mg/g as reported in the papers. The equivalent mg/mmol values are given in Table 24 below. Reagent strip category has also been reported from some studies. It is important to note that the evidence does not differentiate ACR category by sex and thus what was previously termed microalbuminuria is equivalent to an ACR of less than 3mg/mmol in both men and women.

**Table 24: Unit conversion for albuminuria and proteinuria**

| Measure | Units | Normal to mildly increased | Moderately increased | Severely increased |
|---|---|---|---|---|
| ACR | mg/g | <30 | 30-300 | >300 |
| | mg/mmol | <3 | 3-30 | >30 |
| PCR | mg/g | <150 | 150-500 | >500 |
| | mg/mmol | <15 | 15-50 | >50 |

**Summary of included studies**

**Table 25: Summary of studies included in the review**

| Study | Population | Proteinuria measures | Outcomes | Length of follow up (range in years) | Covariates | Study quality |
|---|---|---|---|---|---|---|
| Astor et al. 2011[35] | People with CKD (of diverse clinical diagnoses)<br><br>n = 21,688 | ACR (mg/g)<br>PCR (mg/g)<br>Dipstick category* | End stage kidney disease<br>All-cause mortality | 2.3-9.5 | Age, sex, race, previous cardiovascular disease, smoking status, diabetes mellitus, systolic blood pressure and serum total cholesterol concentration. | High |
| Fox et al. 2012[108] | General population cohorts, high risk cardiovascular cohorts and people with CKD<br><br>Total n = 1,024,977<br>CKD n = 38,612 | ACR (mg/g)<br>PCR (mg/g)<br>Dipstick category* | All-cause mortality<br>Cardiovascular mortality<br>End stage kidney disease | 2.3-24.9 | Age, sex, race (black vs.non-black), smoking, systolic blood pressure, total cholesterol, body-mass index, history of cardiovascular disease, and albuminuria. | High |
| Gansevoort et al. 2011[117] | People at high risk for CKD<br><br>Subgroups: Age (< or > 65 years)<br><br>n = 173,892 | ACR (mg/g)<br>Dipstick category* | Progression of CKD (change in eGFR)<br>End stage kidney disease<br>AKI | 2.3-21.6 | Age, sex, race and cardiovascular risk factors (including cardiovascular disease history, smoking status, diabetes mellitus, systolic blood pressure and serum total cholesterol). | High |
| Hallan et al. 2012[144] | General population cohorts, high risk cardiovascular cohorts and cohorts of people with CKD.<br><br>Subgroups: | ACR (mg/g)<br>PCR (mg/g)<br>Dipstick category* | All-cause mortality.<br>End stage kidney disease. | 2.3-24.9 | Sex, race (black versus non-black) history of cardiovascular disease history, smoking status, diabetes mellitus, systolic blood pressure, serum total cholesterol, BMI, albuminuria and the randomized intervention (for clinical trials). | High |

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| Study | Population | Proteinuria measures | Outcomes | Length of follow up (range in years) | Covariates | Study quality |
|---|---|---|---|---|---|---|
| | Age 18-34, 35-64, 65-74 and ≥75 years.<br><br>Total n = 2,051 244<br><br>CKD n = 38,612 | | | | | |
| Mahmoodi et al.2012[237] | General population cohorts, high risk cardiovascular cohorts and people with CKD<br><br>Total n = 1,127,656<br><br>CKD n = 38,160 | ACR (mg/g)<br>PCR (mg/g)<br>Dipstick category* | All-cause mortality<br>Cardiovascular mortality<br>End stage kidney disease | 2.3-24.9 | Age, sex, race (black vs.non-black), history of cardiovascular disease, diabetes, serum total cholesterol, body mass index, smoking and albuminuria. | High |
| Van der Velde et al. 2011[408] | People at high risk for CKD<br><br>Subgroups: Age (< or > 65 years)<br><br>n = 266,975 | ACR (mg/g)<br>Dipstick category* | All-cause mortality<br>Cardiovascular mortality | 2.3-13.3 | Age, sex, race, cardiovascular disease history, smoking status, diabetes mellitus, systolic blood pressure, and serum total cholesterol. For randomised controlled trials, data were also adjusted for treatment arm. | High |

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** Data reported in evidence tables, but not included in the meta-analyses unless the dipstick category was converted to either ACR or PCR measurement by the study for analysis.*

The reference groups used for calculation of the hazard ratios varied for each of the studies and are given in Table 26 below.

**Table 26: Reference groups for included meta-analyses**

| Study | Reference group for analysis | |
|---|---|---|
| Astor et al. 2011[21] | eGFR 45-74ml/min/1.73 $m^2$ | |
| | Pooled ACR | Stratified by ACR / eGFR |
| Fox et al. 2012[108] | ACR<30mg/g | eGFR 45-74 ml/min/1.73 $m^2$, ACR<10mg/g |
| Gansevoort et al. 2011[117] | N/A | eGFR 60->105 ml/min/1.73 $m^2$, |

| Study | Reference group for analysis | |
|---|---|---|
| | | ACR <10 & 10-29mg/g |
| Hallan et al. 2012[134] | N/A | eGFR 80ml/min/1.73 $m^2$ (50ml/min/1.73 $m^2$ in CKD cohorts)<br>ACR<10mg/g (<20mg/g in CKD cohorts) |
| Mahmoodi et al.2012[237] | ACR<30mg/g | eGFR 45-74 ml/min/1.73 $m^2$, ACR<10mg/g |
| Van der Velde et al. 2011[408] | N/A | eGFR 90-104 ml/min/1.73 $m^2$, ACR <10mg/g |

### 6.1.4 Economic evidence

**Published literature**

No relevant economic evaluations were identified

### 6.1.5 Evidence statements

**Clinical**

***Progression of CKD***

- Evidence from one high quality IPD meta-analysis[117] indicates that there is a trend for worse decline in eGFR with increasing ACR. At eGFR of 15-29ml/min/1.73 $m^2$, only ACR greater than 10mg/g predicts decline in eGFR, although all categories are predictive for eGFR 30-59ml/min/1.73 $m^2$. At eGFR greater than 90ml/min/1.73 $m^2$ there is uncertainty as to whether ACR adds any predictive value.
- Evidence from two high quality IPD meta-analyses[21,117] shows that for all eGFR categories there is a trend for increased occurrence of ESRD with increasing PCR and ACR, however for PCR measures, confidence intervals at each stratification of eGFR overlap. The association is clearer with measures of ACR. When stratified by eGFR, ACR significantly predicts increased risk of ESRD for eGFR 15-29, 30-44 and 45-59ml/min/1.73 $m^2$, but the trend declines at higher eGFRs.
- There is no clear difference between those aged over or under 65 years at any eGFR or ACR, except at eGFR 15-29ml/min/1.73 $m^2$ where increased ACR may be to be more predictive of ESRD for people aged under 65, although confidence intervals are very wide.[408] However, another IPD meta-analysis demonstrated that the association between reduced eGFR and increased risk of progression was decreased with increasing age (greater than 54 years of age), but this was less evident for ACR.[134]
- There is no consistent difference in risk of progression, and confidence intervals are wide for all effect sizes at varying eGFR category or ACR, in people:
  - with or without diabetes,[108] or
  - with or without hypertension.[237]

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***All-cause mortality***

- Evidence from one high quality IPD meta-analysis[21] does not indicate an association with PCR level and incidence of all-cause mortality. Increasing ACR predicts increased all-cause mortality, but differentiation by ACR category is uncertain due to overlapping confidence intervals. When stratified by eGFR[408], the trend decreases as with increasing eGFR category. However, an ACR greater than 30mg/g significantly predicts increased all-cause mortality at all eGFR categories.

- There is no clear difference in risk of all-cause mortality at any category of eGFR or ACR when stratified by either age (over or under 65 years) or presence of diabetes.[108,408] However, another IPD meta-analysis demonstrated that the association between reduced eGFR and increased mortality risk was decreased with increasing age (greater than 54 years of age), but this was less evident for ACR.
- Stratifying by hypertension showed identical results,[237] except for the ACR category 10-29mg/g which appeared to be more predictive of all-cause mortality for people with hypertension, although confidence intervals are very wide. When stratified by eGFR, this difference between populations is no longer apparent.

***Cardiovascular mortality***

- Evidence from one high quality IPD meta-analysis[408] shows that ACR levels greater than 300mg/g are more predictive of cardiovascular mortality than ACR 10-29 or 30-299mg/g, but all are significant. When stratified by eGFR the trend is indicated at all eGFR levels, but decreases with increasing eGFR.
- There is no clear difference in risk of cardiovascular mortality at any category of eGFR or ACR when stratified by age (over or under 65 years) or presence of diabetes or hypertension.

***AKI***

- Evidence from one high quality IPD meta-analysis[117] shows that increasing ACR predicts AKI.

**Economic**

- No relevant economic evaluations were identified.

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### 6.1.6 Recommendations and link to evidence

| | |
|---|---|
| Recommendations | • **Classify CKD using a combination of GFR and ACR categories (as described in Table 27). Be aware that:**<br>o **increased ACR is associated with increased risk of adverse outcomes**<br>o **decreased GFR is associated with increased risk of adverse outcomes**<br>o **increased ACR and decreased GFR in combination multiply the risk ofadverse outcomes. [new 2014]**<br>• **Do not determine management of CKD solely by age. [new 2014]**<br>• **Use the person's GFR and ACR categories (see Table 27) to indicate their risk of adverse outcomes (for example, CKD progression, acute kidney injury, all-cause mortality and cardiovascular events) and discuss this with them. [new 2014]** |
| Relative values of different outcomes | The GDG considered that the critical outcomes for decision making were CKD progression (measured by change in eGFR and occurrence of end stage kidney disease), all-cause mortality, cardiovascular mortality and acute kidney injury (AKI). Cardiovascular events and hospitalisation were considered as important outcomes, but no information was available in this review for these outcomes. |
| Trade off between clinical benefits and harms | The GDG considered that in terms of risk of progression, mortality or risk of developing AKI, there was no difference between CKD stages 1 and 2 in the existing classification system. After careful consideration, it was agreed that in view of the risks of changing this classification system in terms of the confusion it may cause to people that had already been diagnosed, and for clinicians, it would be inappropriate to combine these. However, this is reflected in the classification table demonstating the comparable level of risk by the shading. |

| | |
|---|---|
| Economic considerations | Economic evaluations for the classification of CKD were not applicable given the purely clinical nature of this topic. The GDG considered that an accurate and clear classification of CKD is imperative to facilitate appropriate treatment and management of CKD. The inclusion of risk factors that increase the risk of CKD progression and/or associated adverse outcomes within the classification of CKD does not in itself increase the costs of CKD management for a person. Rather, doing so facilitates more appropriate CKD treatment which can help reduce downstream cost and health consequences. Furthermore, the GDG also considered the negative consequences of stress associated with CKD disease labelling and felt it appropriate to ensure patients with insignificant reduction in kidney function (eGFR >90 ml/min/1.73 $m^2$) did not experience a reduction in their quality of life from a diagnosis of CKD. |
| Quality of evidence | The evidence reviewed was from 5 large high quality IPD meta-analyses. However, it was noted that all of the data were estimated GFR rather than measured GFR values.<br>In addition, the GDG acknowledged the difficulties of interpreting the evidence for adverse outcomes in people who were 'hyperfiltering' (see glossary) and the inability to distinguish those with spuriously high GFRs as a consequence of abnormally low serum creatinine levels (for example due to severe malnutrition or loss of muscle) from those who were truly hyperfiltering. The GDG considered that itwas unlikely that people with high GFRs who were truly hyperfiltering were older (and therefore those who would most likely have severe malnutrition or muscle loss), and it was more likely that these were younger people. |
| Other considerations | There was no evidence that the risk differed in people with hypertension or diabetes, or between males and females, and therefore the GDG agreed that separate recommendations for these populations were not indicated.<br>The GDG were aware that the evidence considered reported ACR as mg/g. When discussing the evidence (in this LETR), for reasons of clarity the GDG refer to the mg/mmol equivalent to conform with UK standard units of measurement for ACR (See Table 24).<br>All outcomes were significantly worse in people with ACR>3 mg/mmol (reported in the evidence as 30 mg/g), this held true for those aged both >65 and <65. Similarly in those with ACR<3 mg/mmol all outcomes were significantly worse for those with eGFR<60 ml/min/1.73 $m^2$, again this was irrespective of age. However, Hallan et al. reported risk of all-cause mortality and end stage kidney disease according to age subgroup. This evidence demonstrated that the risk at any point in time was lower in people aged over 75 than those aged 55-64.[134]<br>The GDG debated the term 'microalbuminuria' in relation to people with diabetes and agreed it was unhelpful to include this term in any classification. The ACR value should be stated specifically to prevent confusion in terminology of what constitutes 'significant proteinuria' and 'microalbuminuria'. Using ACR >3mg/mmol was considered to be more appropriate.<br>The GDG agreed that the data from the CKD prognosis consortia (see classification evidence review, chapter 6.1) indicated that the risk associated with albuminuria rises with increasing albumin creatinine ratio and is evident at levels of ACR below 3mg/mmol. ACR is an independent risk factor for adverse outcomes in people both with and without diabetes mellitus and hypertension.<br>It was noted that a classification incorporating eGFR and ACR categories is rarely used for prescribing, and in this situation GFR category is preferred. The BNF acknowledges that kidney function in adults is reported on the basis of eGFR derived from prediction equations. In the context of drug nephrotoxicity, creatinine clearance is frequently used as a surrogate for GFR. (See recommendation 16) Classification by eGFR and ACR category is more useful in the clinic and for people diagnosed with CKD. The GDG agreed that it was important that people with CKD were made aware that both the eGFR and ACR levels were important, and that this should be highlighted when the classification was explained.<br>The GDG voted to make recommendation 27 a key priority for implementation as |

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they agreed it would have a high impact on outcomes that are important to patient and set challenging but achievable expectations of health services.

The GDG commented that the recommendation will hopefully facilitate the introduction of international classification and risk-based approach to care. They agreed that this recommendation underpinned the rest of the guideline and represents a step forwards in CKD management, although it will need support in implementation. Examples of how this classification would be used are as follows:

- A person with an eGFR of 25 ml/min/1.73 $m^2$ and an ACR of 15 mg/mmol has CKD G4A2.
- A person with an eGFR of 50 ml/min/1.73 $m^2$ and an ACR of 35 mg/mmol has CKD G3aA3.
- An eGFR of less than 15 ml/min/1.73 $m^2$ (GFR category G5) is referred to as kidney failure.

**Table 27: Classification of chronic kidney disease: GFR and ACR categories**

| GFR and ACR categories and risk of adverse outcomes | | | ACR categories (mg/mmol), description and range | | |
|---|---|---|---|---|---|
| | | | <3 Normal to mildly increased | 3–30 Moderately increased | >30 Severely increased |
| | | | A1 | A2 | A3 |
| GFR categories (ml/min/1.73 $m^2$), description and range | ≥90 Normal and high | G1 | No CKD in the absence of markers of kidney damage | | |
| | 60–89 Mild reduction related to normal range for a young adult | G2 | | | |
| | 45–59 Mild–moderate reduction | G3a[1] | | | |
| | 30–44 Moderate–severe reduction | G3b | | | |
| | 15–29 Severe reduction | G4 | | | |
| | <15 Kidney failure | G5 | | | |

Increasing risk

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[1] Consider using eGFRcystatinC for people with CKD G3aA1 (see recommendations 14 and 15)

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

## Malaysia

Iga KNH staadium koos proteinuuriaga oli seotud kahekordse kardiovaskulaarse haigestumise riski ja suremusega. Uuring viidi läbi diabeeti põdevate elanikkonnas, kaasati ka need kelle eGFR on ≥90 ml / min / 1,73.

Patsientidel koos albuminuuriaga oli tunduvalt (85%) suurem risk kardiovaskulaarsesse haigusesse haigestumisel võrreldes ilma albuminuuriata. Samuti näitas uuring,
et albuminuuria suurendab kardiovaskulaarset haigestumust 89% teises staadiumis.

Igal etapil KNH proteinuuria püsimine ennustab selle progresseerumist ja arengut lõppstaadiumis neeruhaiguseks.Ühes Jaapani kohortuuringus, suurendas proteinuuria riski LSNP rohkem kui neli korda.
Elanikkonna uuringute ja meta-analüüside järgi uuritud progresseerumise riski ja proteinuuria taseme põhjal on leitud, et albuminuuria ≥30 mg / mmol tuleks kasutada markerina, sest näitab suurenenud risk KNH progressioonile (võrdub PCR ≥50 mg /mmol või proteinuuria väärtused ≥0.5 g / päevas).

KNH diagnoos eakatel ei tohiks tugineda üksnes eGFR hindamisel. NKF-KDOQI klassifikatsioon võib põhjustada KNH ülediagnoosimist, eriti eakatel. Eakatel patsientidel (vanus> 70 aastat) stabiilse 3a neeruhaigusega ei ole tõenäoline, et neil areneb kroonilise neeruhaigusega seotud komplikatsioone.

**At any stage of CKD, the presence of proteinuria was associated with doubling of CV risk and mortality. In a study conducted in the diabetes population, despite eGFR of ≥90 ml/min/1.73m2, patients with albuminuria had a significantly 85% increased risk of CV events compared to those without albuminuria. Similarly, the study showed that albuminuria increased CV events by 89% in patients with stage 2 disease.50, level II-2**

**At any stage of CKD, persistence of proteinuria predicts its progression and development of ESRD. In a Japanese cohort study, proteinuria significantly increased the risk of ESRD by more than four times. The 7-year cumulative incidence per 1,000 subjects of ESRD gradually increases with declining renal function in stage 3 and 4 of CKD.51, level II-2**

**A study by Hallan Sl et al. demonstrated that combining the effect of GFR and albuminuria for classifying CKD significantly improved prediction of ESRD. The hazard ratio (HR) was 13 if the patient had microalbuminuria compared to 47.2 if the patient had macroalbuminuria.52, level II-2**

**Evidence from longitudinal population studies and meta-analysis of progression risk and level of proteinuria suggested that an ACR ≥30 mg/mmol should be used as a marker for increased risk for progression of CKD (equivalent to a PCR ≥50 mg/mmol or proteinuria values ≥0.5 g/day).53, level II-2; 54, level I**

**Therefore, the suffix (p) is important to be added to denote the presence of proteinuria when staging CKD. A suffix (d) should be added if the patient is on dialysis and (t) should be added if the patient has been transplanted.55, level II**

The diagnosis of CKD in the elderly should not solely rely on eGFR estimation. The NKF-KDOQI classification may lead to overdiagnosis of CKD particularly in the elderly. Elderly patients (age >70 years old) with stable stage 3A of kidney disease are not likely to develop CKD-related complications.[56, level III]

**Clinical audit indicators for quality management proposed are:**

- Percentage of diabetes patients screened for proteinuria/ microalbuminuria = $\frac{\text{Number of diabetes patients screened for proteinuria within a year}}{\text{Total number of diabetes patients on follow-up in the same period}} \times 100\%$
- Percentage of diabetes patients screened for proteinuria = $\frac{\text{Number of hypertensive patients screened for proteinuria within a year}}{\text{Total number of hypertensive patients on follow-up in the same period}} \times 100\%$
- Percentage of diabetic CKD patients with BP <130/80 = $\frac{\text{Number of diabetic CKD patients with BP <130/80 within a year}}{\text{Total number. of diabetic CKD patients in the same period}} \times 100\%$
- Percentage of non-diabetic CKD patients with BP <140/90 = $\frac{\text{Number of non-diabetic CKD patients with BP <140/90 within a year}}{\text{Total number of non-diabetic CKD patients in the same period}} \times 100\%$
- Percentage of patients with hypertension and proteinuria receiving treatment with ACEi or ARB = $\frac{\text{Number of patients with hypertension and proteinuria receiving treatment with ACEi or ARB within a year}}{\text{Total number of hypertension and proteinuria in the same period}} \times 100\%$
- Percentage of patients with diabetes and proteinuria receiving treatment with ACEi or ARB = $\frac{\text{Number of patients with diabetes and proteinuria receiving treatment with ACEi or ARB within a year}}{\text{Total number of diabetes and proteinuria in the same period}} \times 100\%$