Kliiniline küsimus nr 6 ja 7

6. Kas kõiki kroonilise neeruhaiguse riskigrupi patsiente tuleb kroonilise neeruhaiguse ennetamiseks nõustada eluviisi muutmise (toitumine/dieet, suitsetamine, alkoholi tarvitamine, füüsiline aktiivsus) osas vs mitte?

7. Kas kõikidel kroonilise neeruhaigusega patsientidel kasutada parema ravitulemuse saavutamiseks järgmisi sekkumisi vs mitte:
- toitumisnõustamine
- suitsetamisest loobumise nõustamine
- alkoholi tarvitamise piiramise nõustamine
- füüsiline aktiivsuse alane nõustamine

Kriitilised tulemusnäitajad:
6. Tulemusnäitajad: haigestumine kroonilisse neeruhaigusesse, põhihaiguse ravi tulemuslikkus, patsiendi elukvaliteet, patsiendi rahulolu, ravikulu, hospitaliseerimine

7. Tulemusnäitajad: nõustamismeetodi tulemuslikkus, ravisoostumus, patsiendi elukvaliteet, patsiendi rahulolu, kroonilise neeruhaiguse ravi tulemuslikkus, kroonilise neeruhaiguse progresseerumine, hospitaliseerimine, südame-veresoonkonna tüsistused, ravikulu, elulemus, üldsuremuse vähenemine

Otsingusõnad: krooniline neeruhaigus, ülekaal, dieet, suitsetamine, alkohol, valgud, füüsiline aktiivsus, kaalu langetamine, nõustamine
Otsiti andmebaasidest PubMed ja MedLine. Filtriteks kasutati süstemaatilised ülevaated, meta-analüüsid, randomiseeritud-kontrollitud uuringud, viimased 5 aastat, inimesed, tasuta täistekst
Otsingute aeg 27.veebruar kuni 29.märts 2015
Otsing; „chronic kidney disease" [MeSH Terms]) *AND* "alcohol"/ "smoking"/ "diet"/ "weight loss"/"owerweight"/"protein"/"physical activity"/"referral and consultation"/ kokku leitud 255 artiklit, neist sobivateks võetud 11 uuringut
Lisaks andmebaasidest leitud uuringutele kasutati eelnevalt sekretariaadi poolt Agree II meetodil hinnatud ravijuhendeid
Süstemaatilised ülevaated

Kokkuvõte süstemaatilistest ülevaadetest
Süstemaatilistes ülevaadetes käsitletakse riskitegureid koos kroonilise neeruhaiguse diagnoossiga. Süstemaatilisi ülevaateid riskigruppidele ilma KNHta ei leitud.
Leitud 11 uuringust viies on käsitletud toitumisalast nõustamist, nii ülekaalulistel kui ka normkaalulistel, valgu ja soola tarvitamist, samuti diabeeti põdevate inimeste toitumisalast nõustamist. Samuti on käsitletud vererõhu kontrolli vajadust KNH progresseerumise vähendamisel ja südameveresoonkonna haigestumise riski vähendamisel. Kahes artiklis on käsitletud suitsetamise seoseid KNHga ja ühes alkoholi tarvitamise seoseid KNHga. Kahes artiklis kirjeldatakse füüsilise aktiivsuse seoseid KNHga ja ühes artiklis on käsitletud üldist tervislikku elustiili KNH patsientide suremuse vähendamiseks.

Kehakaal ja toitumine
Kriitilises kirjanduse ülevaates metaanalüüsidest (Kiortsis & Christou 2012) käsitletakse ülekaaluliste rasvumisest põhjustatud KNH patsientide seost kaalulanguse ja neerufunktsiooni paranemisega. Põhirõhk on neerufunktsiooni markeritel: albuminuuria, proteinuuria, glomerulaarfiltratsiooni kiirus (GFR) ja kreatiniini kliirens. Kaalujälgimise programm hõlmab

kirurgilist ja mitte-kirurgilist sekkumist (madala kalorsusega dieet, aeroobsed harjutused, ravimitest põhjustatud kaalulangus, kombineeritud ravi). Kaalulanguse sekkumise programmid on osutunud tõhusaks, eriti on langenud proteinuuria, albuminuuria ja vähenenud kõhuõõne rasvkude, need näitajad paranesid rohkem nendel, kelle kaalulangus oli vähemalt 5%. Esmane valik oleks süsivesikutevaene ja madalama kalorisisaldusega dieet, samuti on soovitav pidada kinni üldistest tervislikest eluviisidest. Uuringus on peetud oluliseks alustada kehakaalu langetamist juba varases KNH raskusastmes.

Süstemaatilises ülevaates, mis hõlmab 11 uuringut ja mille hindamiseks kasutati Newcastle-Ottawa skaalat (Van Huffel et al 2014), käsitleti diabeeti ja KNH põdevate inimeste energiavaesema dieedi seoseid suremusele ja kardiovaskulaarse haigestumise riski vähendamisele, Otseseid seoseid ei selgunud, kuid oluliselt vähenes proteinuuria ning oli aeglasem eGFRi langus. Aeroobsete harjutuste suurendamisega langes KMI, kehakaal ja rasvaprotsent, millega seoses paranes füüsiline vorm ja üldine elukvaliteet.
Randomiseeritud uuringus (Campbell at al 2013), mis käsitles kõrge soolasisaldusega toidu tarvitamist vs madala soolasisaldusega toidu tarvitamist KNH inimestel leidsid, et väiksem soola tarvitamine alandab vererõhku ja parandab ka neerufunktsiooni. Vererõhu langus oli rohkem väljendunud KNHga inimestel, sest KNHga inimesed on soolatundlikumad. Väiksema soolasisaldusega toitu tarvitate inimestel vähenes ka vedeliku maht, kehakaal, albuminuuria ja proteinuuria.
Ülevaate artiklist, mis kirjeldas süstemaatilisi ülevaateid ja meta-analüüse (Ash et al 2014) selgus, et toitumissekkumised KNH ravitulemuste parandamiseks ei ole piisavalt tõendatud, kuid valgu piiramine toidus koos keto-analoog ravimitega on tõhus nendel patsientidel kellel on eGFR alla 15 mL/min.'

Suitsetamine.

Süstemaatilistes ülevaadetes (Elihimas Júnior et al 2013; Stack et al 2010), kuhu olid kaasatud kohort-, kliinilised- ja juht-kontrolluuringud, käsitleti suitsetamise seoseid KNH progresseerumisega. Suitsetamine korrelleerus KNH progresseerumisega eriti nendel, kes suitsetasid vähemalt 15 pakki sigarette aastas. Suitsetamine tõstab ka kardiovaskulaarsesse haigusesse haigestumise riski, eriti KNHga inimestel. Suitsetamisest loobumine vähendab suremust ka üldrahvastikus. Uuringutes järeldatakse, et nõustamine ja farmakoteraapia suitsetamisest loobumisel on andnud häid tulemusi, arsti poolt nõustatud inimestest on 30% loobunud suitsetamisest.

Alkoholi tarvitamine

Alkoholi tarvitamise kahju KNHle on uuringutulemustes vastuoluline. Süstemaatilistes ülevaadetes ja meta-enalüüsides (Cheungpasitporn et al 2014) ei leitud olulisi seoseid kõrge alkoholi tarvitamise ja KNH vahel. Tulemuste kvaliteeti piirasid erinevad uurimismeetodid (osad inimesed raporteerisid ise enda alkoholi tarvitamist ja teistega tehti struktueeritud intervjuu).

Füüsiline aktiivsus ja tervislikud eluviisid.

Ühes kliinilises kohortuuringus (Robinson-Cohen et al 2014) käsitleti 3-4 raskusastme KNHga patsientide füüsilise aktiivsuse suurendamise mõju südame ja veresoonkonna funktsiooni parandamisele. Tulemused näitasd, et füüsilise aktiivsuse suurendamine ja elustiili parandamine parandas südametööd, langetas diastoolset vererõhku ja alandas kehakaalu. Teises kliinilises kohortuuringus (Howden et al 2013) osalesid patsiendid, kelle GFR (eGFR) oli 15-59 ml / min per 1,73 m2. Mõõdeti kehalist aktiivsust nelja nädala vältel ja järelkontroll oli 3,7 aasta pärast. Jälgiti eGFRi ja tsüstatiin C muutust. Patsiendid, kes tõstsid füüsilist aktiivsust 60 minuti võrra nädalas langes aastas eGFR ja tsüstatiin C 0,5% vähem võrreldes füüsiliselt vähem aktiivsete uuringus osalejatega.

Tervislikud eluviisid on seotud üldrahvastiku madalama suremuse riskiga. Uuringus, mis oli kihistatud ja rühmitatud, korrigeeritud ristlõike uuring (Ricardo et al 2013) osales 2288 inimest ja hinnati suremust. Uuringus kasutati nii kliinilisi võtteid (vere- ja uriinianalüüsid) kui intervjueerimist. KNH diagnoos oli defineeritud eGFR piiriks 60 ml/min. Uuringus hinnati füüsilist aktiivsust, toitumist, KMId ja suitsetamist. Hindamisel kasutati punktisüsteemil põhinevat kaalutud tervisliku elustiili tulemust. Jälgimisperiood oli 13 aastat.Tulemustes oli suremuse risk väiksem tervislikest eluviisidest kinnipidamisel. Kõige suurem suremuse vähenemise seos oli KNHga mitte suitsetavatel või suitsetamisest loobunutel vs suitsetajatel.

KOKKUVÕTE.

Analüüsitud tõendusmaterjalist selgus, et üldised tervislikud eluviisid on kasulikud nii üldrahvastikule kui KNHga inimesele. Eriti oluline on loobuda suitsetamisest, teha piisavalt aeroobseid treeninguid, jälgida toidu soolasisaldust, hoida vererõhu väärtused normipiires, valida tervislik toit ja hoida kehakaal normipiires. Erinevates uuringutes kasutati terviseprogramme, tervise sekkumisi ja nõustamist/jälgimist spetsialistide poolt. Kõige tugevam seos leiti KNH progresseerumise, suremuse ja suitsetamise vahel. Suitsetamisest loobumine oli tõhusam järjepideva nõustamisega. Alkoholi tarvitamise osas olid tulemused vastuolulised ja kindlaid tõendusmaterjale alkoholi mõjust KNHle ei leitud. Kuna erinevate riskiteguritega patsientidel on erinevad soovitused, siis tervisenõustamist peaks jälgima vastava ala spetsialistid (perearst, dietoloog, füsioterapeut).

Mõnes uuringus (Van Huffel et al 2014; Campbell et al 2012; McMahon et al 2013; Cheungpasitporn et al 2014; Howden et al 2013) oli kvaliteedi piiranguks liiga väike osalejate arv või liiga lühike sekkumise aeg, kuid üldiselt olid uuringud kvaliteetsed süstemaatilised ülevaated, mis olid otsitud suurematest andmebaasides ja mõnele neist oli antud kvaliteedi hinnang.

Viited

Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
Abstract It is well established that obesity is a risk factor for the development of chronic kidney disease (CKD) and may promote the progression to end stage renal disease (ESRD). Therefore, it is strongly suggested that reduction of body weight can be an important intervention in order to reduce the prevalence of renal impairment. The current article describes extensively the already published trials which have studied the association between weight loss and kidney disease. The weight management programs include surgical and non-surgical interventions (low-calorie diet, aerobic exercise, drug-induced weight loss, combination treatment). The focus has been placed on the following renal function markers: albuminuria, proteinuria, glomerular filtration rate (GFR), and creatinine clearance. This review also aims to clarify challenges that clinicians have to deal with in everyday practice regarding the management of obesity-induced kidney disease (degree of weight loss, duration of the weight loss program, early initiation of the intervention).	**Management of Obesity-Induced Kidney Disease: A Critical Review of the Literature; Dimitrios N. Kiortsis Maria A. Christou 2012** Dimitrios N. Kiortsis Maria A. Christou http://www.karger.com/Article/Pdf/345919

Table 2. Effects of weight loss interventions on renal function parameters

Type of intervention	Impact on GFR and/or creatinine clearance	Impact on albuminuria and/or proteinuria	Comments
Diet (5 studies)	+ (1 study) ↔ (2 studies)	↓ (5 studies)	trend towards improvement of GFR and creatinine clearance, especially when the degree of weight loss is significant
Exercise (1 study)	NA	↓	–
Pharmacotherapy (1 study)	NA	↓	orlistat may be more effective to decrease albuminuria in non-diabetics than diabetics
Combination treatment (3 studies)	+ (1 study) – (1 study)	↓ (2 studies)	not well established data about GFR and creatinine clearance, the baseline kidney function probably plays a major role
Bariatric surgery (10 studies)	+ (5 studies)	↓ (8 studies)	significant improvement of renal function in all studies

↔ = No change; + = improvement; – = worsening; ↓ = decrease; NA = not assessed.

It can be concluded that weight loss management programs are effective interventions in order to improve renal disease. Clinicians should assess each patient individually and should also emphasize the benefits of an overall healthy lifestyle. However, further studies should be carefully planned in order to clarify any conflicting data concerning the management of obesity-induced kidney disease.

Background: Obesity and sedentary lifestyle are major health problems and key features to develop cardiovascular disease. Data on the effects of lifestyle interventions in diabetics with chronic kidney disease (CKD) have been conflicting. Study Design: Systematic review. Population: Diabetes patients with CKD stage 3 to 5. Search Strategy and Sources: Medline, Embase and Central were searched to identify papers.
Intervention: Effect of a negative energy balance on hard outcomes in diabetics with CKD. **Outcomes:** Death, cardiovascular events, glycaemic control, kidney function, metabolic parameters and body composition.
Results: We retained 11 studies. There are insufficient data to evaluate the effect on mortality to promote negative energy balance. None of the studies reported a difference in incidence of Major Adverse Cardiovascular Events. Reduction of energy intake does not alter creatinine clearance but significantly reduces proteinuria (mean difference from 20.66 to 21.77 g/24 h). Interventions with combined exercise and diet resulted in a slower decline of eGFR (29.2 vs. 220.7 mL/min over two year observation; p,0.001). Aerobic and resistance exercise reduced HbA1c (20.51 (20.87 to 20.14); p50.007 and 20.38 (20.72 to 20.22); p50.038, respectively). Exercise interventions improve the overall functional status and quality of life in this subgroup. Aerobic exercise reduces BMI (20.74% (21.29 to 20.18); p50.009) and body weight (22.2 kg (23.9 to 20.6); p50.008). Resistance exercise reduces trunk fat mass (20,7□0,1 vs. +0,8 kg□0,1 kg; p50,00120,005). In none of the studies did the intervention cause an increase in adverse events**. Limitations:** All studies used a different intervention type and mixed patient groups. **Conclusions:** There is insufficient evidence to evaluate the

Dietary Restriction and Exercise for Diabetic Patients with Chronic Kidney Disease: A Systematic Review 2014

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4244158/pdf/pone.0113667.pdf

effect of negative energy balance interventions on mortality in diabetic patients with advanced CKD. Overall, these interventions have beneficial effects on glycaemic control, BMI and body composition, functional status and quality of life, and no harmful effects were observed. **Quality assessment** We used the Newcastle-Ottawa Scale to assess the study quality of observational studies. This scale considers a quality score calculated on the basis of three major items: Study participants (0 to 4 points), adjustment for confounding (0 to 2 points) or ascertainment of the exposure or outcome of interest (0 to 3 points) with a maximum score of 9 points which represents the highest methodological quality. The quality of RCTs was assessed using the checklist developed by the Cochrane Renal Group which evaluated the presence of potential selection bias (random sequence generation and allocation concealment), performance bias (blinding of investigators and participants), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data) and reporting bias (selective reporting).	
Background Dietary sodium restriction is a key management strategy in chronic kidney disease (CKD). Recent evidence has demonstrated short-term reduction in blood pressure (BP) and proteinuria with sodium restriction, however the effect on other cardiovascular-related risk factors requires investigation in CKD. **Methods** The LowSALT CKD study involved 20 hypertensive Stage III-IV CKD patients counselled by a dietitian to consume a low-sodium diet (<100 mmol/day). The study was a randomised crossover trial comparing 2 weeks of high-sodium (additional 120 mmol sodium tablets) and low-sodium intake (placebo). Measurements were taken after each crossover arm including BP (peripheral and central), adipokines (inflammation markers and adiponectin), volume markers (extracellular-to-intracellular [E/I] fluid ratio; N-terminal pro-brain natriuretic peptide [NT-proBNP]), kidney function (estimated Glomerular Filtration Rate [eGFR]) and proteinuria (urine protein-creatinine ratio [PCR] and albumin-creatinine ratio [ACR]). Outcomes were compared using paired *t*-test for each cross-over arm. **Results** BP-lowering benefits of a low-sodium intake (peripheral BP (mean±SD) 148/82±21/12 mmHg) from high-sodium (159/87±15/10 mmHg) intake were reflected in central BP and a reduction in eGFR, PCR, ACR, NTproBNP and E/I ratio. There was no change in inflammatory markers, total or high molecular weight adiponectin.	**A randomized trial of sodium restriction on kidney function, fluid volume and adipokines in CKD patients 2012** Katrina L Campbell1,2,3*, David W Johnson1,2,3, Judith D Bauer2, Carmel M Hawley1,2,3, Nicole M Isbel1,2,3, Michael Stowasser1,2,3, Jonathan P Whitehead2,3,4, Goce Dimeski2,5 and Emma McMahon1,2 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3994521/pdf/1471-2369-15-57.pdf

Table 1 Results from a randomized-crossover trial of sodium restriction in hypertensive CKD patients

	Baseline	High sodium	Low sodium
Sodium excretion (mmol/24 hr)#	127 (80–187)	168 (146–219)	75 (58–112)*
Kidney function			
eGFR# (mL/min)	32 (23–42)	39 (23–39)	30 (17–36)*
Serum creatinine# (μmol/L)	184 (135–244)	149 (135–230)	172 (157–276)*
Serum urate# (mmol/L)	0.44 (0.40–0.47)	0.39 (0.34–0.45)	0.46 (0.41–0.51)*
Protein: Creatinine (24 h urine)# (g/mol creat)	49 (12–97)	68 (23–164)	41 (17–126)*
Albumin: Creatinine (24 h urine)# (g/mol creat)	21 (2–65)	27 (5–127)	9 (2–82)*
Volume status			
Extracellular/Intracellular fluid ratio	0.86 ± 0.14	0.92 ± 0.14	0.87 ± 0.13*
Overhydration (L)#	−0.6 (−1.6–1.4)	0.8 (−1.1–2.6)	−0.5 (−1.7–0.9)*
NT–proBNP (pg/mL)#	NA	330 (167–793)	205 (124–528)*
Inflammatory markers			
C-reactive protein (mg/L)#	3.3 (1.6–5.8)	2.8 (1.5–5.5)	2.7 (1.0–7.3)
Interleukin-6 (pg/mL)#	NA	1.9 (1.6–2.8)	1.9 (1.4–2.8)
Interferon-gamma (pg/mL)#	NA	0.8 (0.5–1.1)	1.0 (0.5–1.4)
Tumor necrosis factor – alpha (pg/mL)#	NA	6.8 (5.8–8.7)	7.3 (5.3–9.0)
Total adiponectin (ng/L)	8.1 ± 3.5	7.8 ± 3.6	8.0 ± 3.7
High molecular weight adiponectin (μg/mL)	5.6 ± 3.1	3.9 ± 2.5	3.9 ± 2.6

Data are presented as mean ± standard deviation, median (interquartile range).
NA Data not avaliable.
*p < 0.05 High vs low sodium #log transformed prior to analysis.

Conclusions Short-term benefits of sodium restriction on BP were reflected in significant change in kidney function and fluid volume parameters. Larger, long-term adequately powered trials in CKD are necessary to confirm these results.
Limitations. There are a number of limitations to the present study, some of which, including small sample size and short study duration.

ABSTRACT

There is a paucity of quality evidence regarding the effects of sodium restriction in patients with CKD, particularly in patients with pre-end stage CKD, where controlling modifiable risk factors may be especially important for delaying CKD progression and cardiovascular events. We conducted a doubleblind placebo-controlled randomized crossover trial assessing the effects of high versus low sodium intake on ambulatory BP, 24-hour protein and albumin excretion, fluid status (body compositionmonitor), renin and aldosterone levels, and arterial stiffness (pulse wave velocity and augmentation index) in 20 adult patients with hypertensive stage 3–4 CKD as phase 1 of the LowSALT CKD study. Overall, saltrestriction resulted in statistically significant and clinically important reductions in BP (mean reduction of systolic/diastolic BP, 10/4 mm Hg; 95% confidence interval, 5 to 15 /1 to 6 mm Hg), extracellular fluid volume, albuminuria, and proteinuria in patientswithmoderate-to-severe CKD. The magnitude of change
was more pronounced than the magnitude reported in patients without CKD, suggesting that patients withCKDare particularly salt sensitive. Although studieswith longer intervention times and larger sample
sizes are needed to confirm these benefits, this study indicates that sodium restriction should be emphasized in the management of patients with CKD as a means to reduce cardiovascular risk and risk for CKD progression.

Results

A Randomized Trial of Dietary Sodium Restriction in CKD 2013

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http://jasn.asnjournals.org/content/24/12/2096.full.pdf+html

Table 2. Values during low salt and high salt periods (*n*=20)

Characteristics	*n*	High Salt	Low Salt	Δ (High Salt – Low Salt)	*P*
24-h systolic BP (mmHg)	20	154.6±11.9	144.9±13.1	9.7 [4.5 to 14.8]	<0.001
24-h diastolic BP (mmHg)	20	83.3±9.0	79.4±9.4	3.9 [1.3 to 6.4]	<0.01
24-h mean arterial pressure (mmHg)	20	106.7±8.7	100.9±9.7	5.8 [2.6 to 9.1]	<0.01
Maximum systolic BP (mmHg)	20	212.7±25.7	198.9±26.6	13.8 [0.5 to 27.1]	0.04
Extracellular volume (L)	18	20.0±3.7	19.2±3.7	0.8 [0.4 to 1.2]	<0.01
Weight (kg)	20	86.4±12.6	86.0±12.2	0.4 [0.0 to 0.8]	0.03
Plasma renin (pmol/L)	20	16.5 (8.5–47.0)	64.5 (32.0–117.5)	−48 (−70.5, −23.5)	<0.001
Plasma aldosterone (mU/L)	20	33.3 (25.0–58.8)	87.1 (29.8–133.5)	−53.8 (−74.7, −4.8)	<0.001
Proteinuria (mg/24 h)	19	835 (185–1600)	493 (123–1300)	342 (62, 300)	<0.01
Albuminuria (mg/24 h)	19	291 (40–1000)	143 (16–889)	148 (24, 111)	<0.001
PWV (m/s)	16	11.1±2.3	10.5±2.5	0.5 [−0.2 to 1.2]	0.13
AI (%)	19	28.9±8.8	27.2±11.5	1.7 [−2.6 to 6.0]	0.42
Sodium excretion (mmol/24 h)	19	168 (146–219)	75 (58–112)	93 (88, 107)	<0.001
Potassium excretion (mmol/24 h)	19	57±18	57±21	0 [−6 to 6]	0.91
Energy intake (from diet history)	20	6600±1400	6800±1500	−200 [−700 to 300]	0.32
Sodium intake (from diet history)[a]	20	53 (43–66)	56 (48–63)	3 (−5, 3)	0.31

Data are presented as the mean ± SD, median (interquartile range), or mean [95% confidence interval]. The change between interventions was analyzed using the paired *t* test with normally distributed data and the Wilcoxon signed-rank test for non-normal data.
[a]Does not include sodium from study medication.

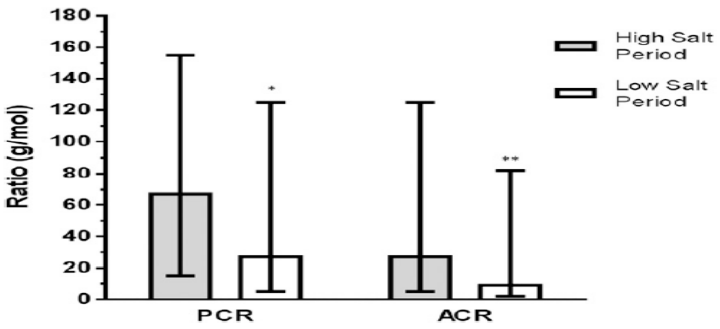

Figure 4. Median urinary protein/creatinine ratio (PCR) and albumin/creatinine ratio (ACR) during the high salt and low salt periods. Error bars indicate interquartile range.*$P<0.01$; **$P<0.001$ for difference from high salt period. PCR and ACR were significantly reduced on a low-sodium diet compared with a high-sodium diet.

Design

After baselinemeasurements were taken, participants were counseled to follow a low-sodium diet (goal 60–80mmol) for the 6-week study. Dietary education was individualized to the participant's food preferences and was provided by an accredited practicing dietitian. Participants were also offered a variety of low-sodium foods (one preprepared meal per day, snack foods, breakfast cereal, cheese, and bread) throughout the study. After a 1-week run-in period on a low-sodium diet, participants were randomized to high sodium intake (low-sodium diet with a goal of 60–80 mmol, plus 120 mmol sodium per day via slow-release sodiumtablets) or low sodium intake (low-sodiumdiet with a goal of 60–80mmol, plus a matched quantity of placebo capsules) for 2 weeks. After a 1-week washout (continued low-sodium diet), patients crossed over to the other intervention. The target total sodium intakes (dietary intake plus study medication) were 180–200 mmol in the high salt period and 60–80 mmol in the low salt period. Randomization was performed by an external statistical consultant, with the study medication packaged offsite and labeled with the study numbers and intervention order. Participants, investigators, and outcome assessors were blinded to the allocation.

Limitation.

Given that this study was designed as a proof of concept, limitations to

translating these findings to practice include the short intervention duration, difference in baseline characteristics between completers and withdrawers, and small sample size.	
Abstract: In Chronic Kidney Disease (CKD), management of diet is important in prevention of disease progression and symptom management, however evidence on nutrition prescription is limited. Recent international CKD guidelines and literature was reviewed to address the following question *"What is the appropriate nutrition prescription to achieve positive outcomes in adult patients with chronic kidney disease?"* Databases included in the search were Medline and CINAHL using EBSCOhost search engine, Embase and the Cochrane Database of Systematic Reviews published from 2000 to 2009. International guidelines pertaining to nutrition prescription in CKD were also reviewed from 2000 to 2013. Three hundred and eleven papers and eight guidelines were reviewed by three reviewers. Evidence was graded as per the National Health and Medical Research Council of Australia criteria. The evidence from thirty six papers was tabulated under the following headings: protein, weight loss, enteral support, vitamin D, sodium, fat, fibre, oral nutrition supplements, nutrition counselling, including protein and phosphate, nutrients in peritoneal dialysis solution and intradialytic parenteral nutrition, and was compared to international guidelines. While more evidence based studies are warranted, the customary nutrition prescription remains satisfactory with the exception of Vitamin D and phosphate. In these two areas, additional research is urgently needed given the potential of adverse outcomes for the CKD patient. **Conclusions** Overall, the body of evidence supporting nutritional interventions for improving patient outcomes in CKD is primarily based on low level evidence or isolated randomized clinical trials. Much of the evidence around dietary prescription relies on retrospective and uncontrolled cohort studies and the quality of the body of evidence is poor. Most outcomes assessed are generally biochemical endpoints, such as change in serum levels, rather than clinical ones, such as mortality, hospitalization, cost and patient quality of life. There is general agreement across guideline recommendations for the levels of protein in early CKD and on dialysis; however, guidance on the use of very low protein diets with keto-analogues in conservative treatment of those with GFR < 15 mL/min is warranted. **GRADING**	**Nutrition Prescription to Achieve Positive Outcomes in Chronic Kidney Disease: A Systematic Review 2014** Susan Ash 1,*, Katrina L. Campbell 2, Jessica Bogard 3 and Anna Millichamp 3 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3916870/pdf/nutrients-06-00416.pdf

Appendix 1. Grading of evidence for different guidelines.

Grading Body	Best evidence (A/1A/Strong)	Good Evidence (B/Fair)	Mixed Evidence (C)	Weak Evidence (D)	
	A—Excellent	**B—Good**	**C—Satisfactory**	**D—Poor**	
NHMRC. National Health and Medical Research Council, Australia (2009) [20]	Body of evidence can be trusted to guide practice. Several level I or II studies with low risk of bias; Excellent consistency across studies; Very large clinical impact; Results are directly generalisable to target population; Results are directly applicable to the Australian healthcare context.	Body of evidence can be trusted to guide practice in most situations. One or two level II studies with low risk of bias or systematic review of multiple level III studies with low risk of bias. Most studies are consistent and inconsistencies can be explained. Substantial clinical impact; Results are directly generalisable to target population with some caveats; Results are directly applicable to the Australian healthcare context with few caveats.	Body of evidence provides some support for recommendation(s) but care should be taken in its application. Satisfactory level III studies with low risk of bias or level I or II studies with moderate risk of bias. Some inconsistency reflecting genuine uncertainty around question. Moderate clinical impact; Not directly generalisable to target population but could be sensibly applied. Results are probably applicable to the Australian healthcare context with some caveats.	Body of evidence is weak and recommendation must be applied with caution. Level IV studies or level I to III studies with high risk of bias. Evidence is inconsistent; Slight or restricted clinical impact. Not directly generalisable to target population hard to judge whether it is sensible to apply. Results are not applicable to the Australian healthcare context.	
	A	**B**	**C**	**D**	**Good Practice Points**
SIGN Scottish Intercol-legiate Guidelines Network 2008 [12]	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; OA body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; OR; Extrapolated evidence from studies rated as 1++ or 1+.	A body of evidence including studies rated as 2+, directly applicable to the target population, and demonstrating overall consistency of results; OR; Extrapolated evidence from studies rated as 2++.	Evidence level 3 or 4; Extrapolated evidence from studies rated as 2+.	Recommended best practice based on the clinical experience of the guidelines development group.
Canadian Society Nephrology (2008) [11]	High quality RCT or meta-analyses with adequate power and clinically important outcomes.	High quality RCT or meta-analyses with adequate power but outcome is a validated surrogate or results need to be extrapolated from study population to real population OR; High quality RCT or meta-analyses with inadequate power but with clinically important or validated surrogate outcome	High quality RCT or meta-analyses with adequate power but outcome is neither clinically important or a validated surrogate outcome OR; Observational study with statistically significant results and outcome is clinically important or a validated surrogate AND study population is representative of population recommendation is for OR results can be extrapolated from study population to real population.	High quality RCT or meta-analyses with inadequate power and neither clinically important nor validated surrogate outcomes OR; Observational study with statistically significant results but neithe clinically important nor validated surrogate outcome OR; Observational study with inadequate power and applicability of th study is irrelevant.	
	A High	**B Moderate**	**C Low**	**D Very Low**	
KDIGO Kidney Disease Improving Global Outcomes (2013) [5]	We are confident that the true effect lies close to that of the estimate of the effect. Level 1 "We recommend". Most people in situation would want the recommended course of action and only a small proportion would not. The recommendation can be evaluated as a candidate for developing a policy or a performance measure.	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Level 2 "We suggest"; The majority of people *in situation* would want the recommended course of action, but many would not. The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.	The true effect may be substantially different from the estimate of the effect.	The estimate of effect is very uncertain, and often will be far from the truth.	

	A	B	C
KDOQI. National Kidney Foundation—Kidney Disease Outcome Quality Initiative (2002) [61]	It is strongly recommended that clinicians routinely follow the guidelines for eligible patients. There is strong evidence that the practice improves health outcomes.	It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderately strong evidence that the practice improves health outcomes	It is recommended that clinicians consider following the clinical practice recommendation for eligible patients. This recommendatio is based on either weak evidence or on the opinions of the work gr and reviewers that the practice might improve health outcomes.

	Strong	Fair	Weak	Consensus
ADA. American Dietetic Association (2010) [18]	The workgroup believes the benefits of the recommended approach clearly exceed the harms (or that harms clearly exceed benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent/good (grad I or II).	The workgroup believes the benefits exceed the harms (or that harms clearly exceed benefits in the case of a strong negative recommendation) but the quality of evidence is not as strong (grade II or III)	Quality of evidence that exists is suspect or well done studies (grade I, II or III) show little clear advantage to one approach *versus* another. Patient preferences should have a substantial influencing role in patient care.	A consensus recommendation means that expert opinion (gra IV) supports the guideline recommendation even though available scientific evidence di not present consistent results, controlled trials were lacking.

	1A	2A	1B	2B	1C	1D	1D	2D
CARI Caring for Australians with Renal Impairment (2013) [15]	Strong recommendation High quality evidence. Consistent evidence from well performed RCTs or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk. Strong recommendations can apply to most patients in most circumstances without reservation.	Weak recommendation High quality evidence. Consistent evidence from well performed RCTs or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk. Clinicians should follow a strong recommendation unless there is a clear rationale for an alternative approach.	Strong recommendation. Moderate quality evidence. Evidence from RCTs with important limitations (inconsistent results, methods flaws, indirect or imprecise), or very strong evidence of some other research design. Further research may impact on our confidence in the estimate of benefit and risk. Strong recommendation and applies to most patients.	Weak recommendation. Moderate quality evidence. Evidence from RCTs with important limitations (inconsistent results, methods flaws, indirect or imprecise), or strong evidence of some other research design. Further research may change the estimate of benefit and risk. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.	Strong recommendation. Low quality evidence. Evidence from observational studies, unsystematic clinical experience, or from RCTs with serious flaws. Any estimate of effect is uncertain. Strong recommendation, and applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.	Weak recommendation. Low quality evidence. Evidence from observational studies, unsystematic clinical experience, or from RCTs with serious flaws. Any estimate of effect is uncertain.	Strong recommendation. Very low quality evidence; Evidence limited to case studies. Strong recommendation based mainly on case studies and expert judgement.	Weak recommendation. Ver low quality evidence Evidence limited to case stu and expert judgement Very weak recommendation other alternatives may be eq reasonable.

Appendix 1. *Cont.*

	High	Moderate	Low	Very low
Grading of Recommendations Assessment Development Evaluation (GRADE) [59]	We are very confident that the true effect lies close to that of the estimate of the effect. Further research is very unlikely to change our confidence in the estimate of effect.	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	We have very little confidence in the effect estimate: The true is likely to be substantially different from the estimate of effect estimate of effect is very uncertain.

Introduction: Chronic kidney disease (CKD) and smoking are public health problems. **Objective:** To assess smoking as a risk factor for progression of CKD. **Methods:** We conducted a systematic review in Medline, LILACS, SciELO, Google Scholar, Embase and Trials.gov with articles published until February/2013. Were included: cohort, clinical trials and case-control. Performed in humans, aged ≥ 18 years with smoking as a risk factor for progression of CKD. We excluded studies that reported no smoking and CKD in the title or had proposed to reduce smoking. **Results:** Among 94 citations, 12 articles were selected. Of these, six were multicenter conducted in developed countries, four were randomized. Males predominated 51-76%. There was associated with smoking progression in 11 studies. It was found that the consumption ≥ 15 packs/ year increases the risk of progression of CKD. **Conclusion:** Smoking is a

Smoking as risk factor for chronic kidney disease: systematic Review 2013

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Helen Conceição dos Santos Elihimas,
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risk factor for progression of CKD. This systematic review revealed a correlation between smoking and progression of CKD. This positive correlation became more pronounced for individuals smoking 15 of more packs of cigarettes a year. **Smoking and clinical practice** Regardless of the mechanism of renal injury, the evidence derived from observational studies indicates that CKD patients with comorbidities (primary glomerulonephritis, 16 COPD,20 hypertension,25 HIV,24 proteinuria28) tend to experience faster declines in GFR and increased risk of death. 44,45 The evidence on CKD progression, mortality, tobacco dose-effect, and renal function deterioration leaves no doubt over the need to combat smoking.	Eduardo Eriko Tenório de França, Andrea Lemos, Lucila Maria Valente, Brivaldo Markman Filho http://www.scielo.br/pdf/jbn/v36n4/en_0101-2800-jbn-36-04-0519.pdf
ABSTRACT Tobacco use is a majormodifiable cardiovascular risk factor in the general population and contributes to excess cardiovascular risk. Emerging evidence from large-scale observational studies suggests that continued tobacco use is also an independent cardiovascular risk factor among patients with chronic kidney disease (CKD). The benefits of smoking cessation programs on improving the heath status of patients and reducing mortality are unequivocal in the general population. Despite this, there has been little effort in pursuing tobacco cessation programs in dialysis cohorts or those with lesser degrees of kidney impairment.Most of our attention to date has focused on the development of ‘‘kidney-specific’’ interventions that reduce rates of renal disease progression and improve dialysis outcomes. The purpose of this current review is to describe the epidemiology of tobacco use among patients with CKD, draw attention to its negative impact on cardiovascular morbidity and mortality, and finally highlight potential strategies for successful intervention. We hope that this study heightens the importance of tobacco use inCKD, stimulates renewed interest in the barriers and challenges that exist in achieving smoking cessation, and endorses the efficacy of intervention strategies and the immeasurable benefits of quitting on cardiovascular and noncardiovascular outcomes.	**Cigarette Use and Cardiovascular Risk in Chronic Kidney Disease: An Unappreciated Modifiable Lifestyle Risk Factor 2010** Austin G. Stack, Bhamidipati V. R. Murthy http://onlinelibrary.wiley.com/doi/10.1111/j.1525-139X.2010.00728.x/pdf
Background: The risk of renal damage in patients with high alcohol consumption is controversial. The objective of this meta-analysis was to evaluate the associations between high alcohol consumption and progression of kidney damage including chronic kidney disease (CKD), end-stage renal disease (ESRD) and proteinuria. **Methods:** A literature search was performed using MEDLINE, EMBASE and Cochrane Databases from inception through August 2014 to identify studies investigating the association between high alcohol consumption and CKD, ESRD or proteinuria. Studies that reported odds ratios, relative risks or hazard ratios comparing the risk of CKD, ESRD or proteinuria in patients consuming high amount of alcohol versus those who did not consume alcohol were included. Pooled risk ratios (RRs) and 95% confidence interval (CI) were calculated using a random-effect, generic inverse variance method. **Results:** Twenty studies with 292 431 patients were included in our analysis to assess the associations between high alcohol consumption and progression of kidney damage. The pooled RRs of CKD, proteinuria and ESRD in patients with high alcohol consumption were 0.83 (95% CI: 0.71–0.98), 0.85 (95% CI: 0.62–1.17) and 1.00 (95% CI: 0.55–1.82), respectively. Post hoc analysis assessing the sex-specific association between high alcohol consumption and CKD demonstrated pooled RRs of 0.72 (95% CI: 0.57–0.90) in males and 0.78 (95% CI: 0.58–1.03) in females. **Conclusions:** Our study demonstrates an inverse association between high	**High alcohol consumption and the risk of renal damage: a systematic review and meta-analysis 2014** W. Cheungpasitporn, C. Thongprayoon , W. Kittanamongkolchai , B.A. Brabec , O.A. O'Corragain , P.J. Edmonds , S.B. Erickson 'http://qjmed.oxfordjournals.org/content/qjmed/early/2014/12/22/qjmed.hcu247.full.pdf

alcohol consumption and risk for developing CKD in males. There is no significant association between high alcohol consumption and the risk for developing proteinuria or ESRD. **Limitations**. Although all included studies were of moderate to high quality (as evaluated by Newcastle-Ottawa scale), there are some limitations. Firstly, some studies were conducted based on self-report, not a structured interview or medical record review. Although some studies have validated the use of self-reported alcohol consumption, under-reporting for alcohol consumption has been found especially in heavy alcohol drinkers	
Physical activity may counteractmetabolic disturbances that promote the progression of CKD. To address this concept, we performed a longitudinal cohort study of 256 participants in the Seattle Kidney Study, a clinic-based study of CKD. Participants with an estimated GFR (eGFR) of 15–59 ml/min per 1.73 m2 at baseline were eligible for the study. Physical activity was quantified using the Four-Week Physical Activity History Questionnaire.We used generalized estimating equations to test associations of physical activity with change in eGFR determined by longitudinal measurements of serum cystatin C. Mean baseline eGFR was 42 ml/min per 1.73 m2. During a median 3.7 years of follow-up, the mean change in eGFRcystatin C was 27.6% per year (interquartile range, 216.8%, 4.9% per year). Participants who reported .150 minutes of physical activity per week had the lowest rate of eGFRcystatin C loss (mean 26.2% per year compared with 29.6% per year among inactive participants). In adjusted analyses, each 60-minute increment in weekly physical activity duration associated with a 0.5%slower decline per year in eGFR (95%confidence interval, 0.02 to 0.98; P=0.04). Results were similar in sensitivity analyses restricted to participants without cardiovascular disease or diabetes, or to participants with moderate/high physical function. After adjustment for eGFR at the time of questionnaire completion, physical activity did not associate with the incidence of ESRD (n=34 events). In summary, higher physical activity levels associatedwith slower rates of eGFR loss in persons with established CKD.	**Physical Activity and Change in Estimated GFR among** **Persons with CKD 2013** Cassianne Robinson-Cohen, Alyson J. Littman, Glen E. Duncan, Noel S. Weiss, Michael C. Sachs, John Ruzinski, John Kundzins, Denise Rock, Ian H. de Boer, T. Alp Ikizler, Jonathan Himmelfarb, and Bryan R. Kestenbaum http://jasn.asnjournals.org/content/25/2/399.full.pdf+html

Results

Table 2. Association of physical activity and annualized relative change in eGFR cystatin C

Leisure-Time Physical Activity Level (min/wk)	Percent Annual Change in eGFR Cystatin C (95% Confidence Interval)			
	Unadjusted	Model 1[a]	Model 2[b]	Model 3[c]
None	−9.6 (−12.0 to −7.1)	−10.1 (−12.4 to −7.7)	−9.4 (−11.8 to −6.9)	−9.4 (−12.0 to −6.9)
1–59	−8.2 (−10.3 to −6.1)	−8.0 (−10.0 to −6.0)	−8.1 (−10.2 to −6.0)	−8.7 (−10.9 to −6.5)
60–150	−6.8 (−9.4 to −4.3)	−7.1 (−9.5 to −4.7)	−7.2 (−9.7 to −4.7)	−8.4 (−10.7 to −6.2)
≥150	−6.2 (−8.3 to −4.2)	−5.9 (−7.9 to −3.9)	−6.4 (−8.4 to −4.3)	−6.6 (−8.8 to −4.4)
P value for trend	0.02	0.02	0.03	0.05
Per 60 min/week increment	1.3 (0.23 to 2.32)	0.61 (0.14 to 1.07)	0.52 (0.03 to 1.00)	0.50 (0.02 to 0.98)

P values for continuous association (per 60 min/wk increment in physical activity) were 0.02, 0.01, 0.03, and 0.04 for the unadjusted model and models 1, 2, and 3, respectively.
[a]Model 1 is adjusted for age, race, sex, and study site.
[b]Model 2 is adjusted for the variables in model 1 plus education, body mass index, diabetes, smoking status, alcohol, and prevalent coronary artery disease.
[c]Model 3 is adjusted for the variables in model 2 plus hemoglobin A1c, systolic BP, angiotensin-converting enzyme inhibitor use, angiotensin-receptor blocker use, statin use, and C-reactive protein.

Background and objectives CKD is associated with poor cardiorespiratory fitness (CRF). This predefined
substudy determined the effect of exercise training and lifestyle intervention on CRF and explored the effect on
cardiovascular risk factors and cardiac and vascular function.
Design, setting, participants, &measurements Between February 2008 and March 2010, 90 patients with stage 3–4
CKD were screenedwith an exercise stress echocardiogram before enrollment. Patients (n=83)were randomized
to standard care (control) or lifestyle intervention. The lifestyle intervention included multidisciplinary care
(CKD clinic), a lifestyle program, and aerobic and resistance exercise training for 12 months. CRF (peak V_ O2), left
ventricular function, arterial stiffness, anthropometric, and biochemical data were collected at baseline and 12
months.
Results Ten percent of randomized patients had subclinical myocardial ischemia at screening and completed the
study without incident. There was no baseline difference among 72 patients who completed follow-up (36 in the
lifestyle intervention group and 36 in the control group). The intervention increased peak V_ O2 (2.860.7 ml/kg
per minute versus 20.360.9 ml/kg per minute; P=0.004). There was small weight loss (21.864.2 kg versus
0.763.7 kg; P=0.02) but no change in BP or lipids. Diastolic function improved (increased e' of 0.7561.16 cm/s
versus 20.4761.0 cm/s; P=0.001) but systolic function was well preserved and did not change. The change in
arterial elastance was attenuated (0.1160.76 mmHg/ml versus 0.7660.96 mmHg/ml; P=0.01). D peak V_ O2 was
associated with group allocation and improved body composition.
Conclusions Exercise training and lifestyle intervention in patients with CKD produces improvements in CRF,
body composition, and diastolic function.

Effects of Exercise and Lifestyle Intervention on Cardiovascular Function in CKD 2013

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http://cjasn.asnjournals.org/content/8/9/1494.full.pdf+html

Background and objective Among general populations, a healthy lifestyle has been associated with lower risk
of death. This study evaluated this association in individuals with CKD. Design, setting, participants,&measurementsAtotal of 2288 participantswithCKD(estimatedGFR,60 ml/min per 1.73m2 ormicroalbuminuria) in the ThirdNationalHealth andNutrition Examination Surveywere included.
A weighted healthy lifestyle score was calculated (range, 24 to 15, with 15 indicating healthiest lifestyle) on the
basis of the multivariable Cox proportional hazards model regression coefficients of the following lifestyle
factors: smoking habit, bodymass index (BMI), physical activity, and diet.Main outcomewas all-causemortality,
ascertained through December 31, 2006.

Table 1. Point-based system to calculate weighted healthy lifestyle score

Characteristic	Points Based on Regression Coefficients
BMI	
18.5 to <22 kg/m^2	−4
22 to <25 kg/m^2	0
25 to <30 kg/m^2	0
≥30 kg/m^2	2
Physical activity	
Inactive	0
Insufficient	2
Recommended	3
Smoking	
Current	0
Past	7
Never	9
Healthy Eating Index score	
<54.4	0
54.5 to <63.7	0
63.8 to <73.1	0
73.1–100	1

Results Aftermedian follow-up of 13 years, 1319 participants had died. Compared with individuals in the lowest
quartile of weighted healthy lifestyle score, adjusted hazard ratios (95% confidence intervals) of all-cause
mortality were 0.53 (0.41–0.68), 0.52 (0.42–0.63), and 0.47 (0.38–0.60) for individuals in the second, third, and
fourth quartiles, respectively. Mortality increased 30% among individuals with a BMI of 18.5 to ,22 kg/m2
versus 22 to ,25 kg/m2 (P,0.05); decreased mortality was associated with never-smoking versus current
smoking (0.54 [0.41–0.70]) and regular versus no physical activity (0.80 [0.65–0.99]). Diet was not significantly
associated with mortality.
Conclusions Compared with nonadherence, adherence to a healthy lifestyle was associated with lower all-cause
mortality risk in CKD. Examination of individual components of the healthy lifestyle score, with adjustment for
other components, suggested that the greatest reduction in all-cause mortality was related to nonsmoking.

Adherence to a Healthy Lifestyle and All-Cause Mortality in CKD 2013

Ana C. Ricardo, Magdalena Madero, Wei Yang, Cheryl Anderson, Matthew Menezes, Michael J. Fischer,
Mary Turyk, Martha L. Daviglus, and James P. Lash

http://cjasn.asnjournals.org/content/8/4/602.full.pdf

Ravijuhendid

Kokkuvõte ravijuhendites leiduvast

<u>Küsimus 6</u>

KHA-CARI

Riskigruppidele hüpertoonia, diabeet, ülekaal, suitsetajad jt. riskitegurid.

*Ravijuhend soovitab jälgida kehakaalu, soovituslik normkaalust kõikumine 5% ulatuses. Normkaaluga on väiksem tõenäosus haigestuda KNHsse (2C).
*Kaalu langetamiseks farmakoloogiliste preparaatide kasutamine kombinatsioonis mitte medikamentoossete meetoditega vähendab riski haigestuda KNHsse (2B).
*Madala soolasisaldusega dieet (2,3 g/päevas) vähendab haigestumise riski (2C).
*Valgu tarbimise suhteline kasu vs kahju ei ole piisavalt tõestatud (2D).

Elustiili muutmine riskirühmadel.

*Suitsetamisest loobumisel ja alkoholi liigtarvitamisel on vajalik pakkuda psühholoogilist abi.
*Regulaarne füüsiline aktiivsus peab olema sobiv arvestades patsiendi füüsilist vormi, võimeid ja haiguse anamneesi.
*Vererõhu kontroll 1 x aastas, soovituslikult saada VR <140/90 mmHg tasemele (1A).
*Diabeetikutel: regulaarne kehaline aktiivsus, VR, kolesterooli ja veresuhkru pidev kontroll.
*Diabeetikutel soovitav jälgida VR väärtusi ka kodus (1C).

NICE

*Kaalujälgimine, tervislik toitumine, regulaarne füüsiline aktiivsus ja mitte suitsetamine on kasulik kõigile ja eriti oluline inimestele, kellel on südame-veresoonkonna haigused.
*Puudusid tõendid KNH diagnoosiga inimestele, kes suitsetavad suurema risk osas haigestuda südame-veresoonkonna haigustesse, võrreldes suitsetavate ilma kroonilise neeruhaiguseta inimestega.
*Puudusid tõendid kahjulike mõjude kohta alkoholi tarvitamisel haigestumisega KNHsse.

<u>Küsimus 7</u>

CKD Malaysia

*Soovituslik valgu piiramine toidus 0,6-0,8 g/kg/päevas ja piisav energia tarbimine päevas 30-35 kcal/kg/päevas 3.-5. KNH raskusastmega haigetel. Valgu piiramist peab jälgima dietoloog. (Grade B). Valgu tarbimine väljendunud mikroalbuminuuria ja proteinuuria puhul 0,8-1,0 g/kg/päevas.
*Naatriumi piiramist tuleks KNHga patsientidel alustada 2,4 g/päevas, sest Na+ tarbimine on otseses seoses albuminuuria süvenemisega.
*KNH patsiente tuleks nõustada kaalulangetamisel ja suitsetamisest loobumisel. (Grade B).
*Alkoholi tarvitamise mõju kohta KNH patsientidel on uuringutes olnud erinevad tulemused ja ei ole otseseid tõendeid alkoholi mõjust KNH progresseerumisele, kuid KNH patsientidel on mõistlik alkoholi tarvitamist vähendada.

LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II -1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

GRADES OF RECOMMENDATION

A	At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population
B	Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT
C	Evidence from expert committee reports, or opinions and /or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality

NICE CKD 2014

*Vähese valgusisaldusega dieeti ei soovitata kõikidele KNH patsientidele, peab vaatama vanust, eGFRi, diabeeti jm. tegureid. Uuringutes on leitud seos KNH progresseerumise ja suitsetamise vahel, ka peale kohandamist diabeediga.

*KNH patsientidile tuleks soovitada langetada ülekaalu ja loobuda suitsetamisest.

*Toitumissoovitustes jälgida kaaliumi, fosfori, kalorite ja soola tarvitamist. Kaaliumi, fosfori, kalorite ja soola tarvitamist peaks jälgima toitumisspetsialist.

Table 3: Description of quality elements in GRADE for intervention studies

Quality element	Description
Limitations	Limitations in the study design and implementation may bias the estimates of the treatment effect. Major limitations in studies decrease the confidence in the estimate of the effect.
Inconsistency	Inconsistency refers to an unexplained heterogeneity of results.
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question, or recommendation made.
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of the effect relative to the clinically important threshold.
Publication bias	Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies.

Table 4: Levels of quality elements in GRADE

Level	Description
None	There are no serious issues with the evidence.
Serious	The issues are serious enough to downgrade the outcome evidence by one level.
Very serious	The issues are serious enough to downgrade the outcome evidence by two levels.

Table 5: Overall quality of outcome evidence in GRADE

Level	Description
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Grading the quality of clinical evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start HIGH and observational studies as LOW, uncontrolled case series as LOW or VERY LOW.
2. The rating was then downgraded for the specified criteria: Study limitations, inconsistency, indirectness, imprecision and reporting bias. These criteria are detailed below. Observational studies were upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have "serious" or "very serious" risk of bias were rated down -1 or -2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW or VERY LOW if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

The details of criteria used for each of the main quality elements are discussed further in the following sections 3.1.4.5 to 3.1.4.8

KHA-CARI

*Soovitab jälgida kehakaalu, soovituslik normkaalust kõikumine 5% ulatuses (2C).

*Madala soolasisaldusega toit (2,3 g/päevas) KNH progresseerumise vähendamiseks. Valgu tarbimise suhteline kasu vs kahju ei ole piisavalt tõendatud.

*Suitsetamisest loobumisel ja alkoholi liigtarvitamisel pakkuda psühholoogilist abi.
*Regulaarne füüsiline aktiivsus peab olema sobiv arvestades patsiendi füüsilist vormi, võimeid ja haiguse anamneesi.
*Vererõhu kontroll: 1.-2. KNH raskusastmete patsientidel VR kontroll 1 kord aastas, soovituslikult saada VR < 140/90 tasemele.
*Patsientidel KNH raskusastmetes 3a, 3b VR kontroll iga 3-6 kuu tagant.
*KNH haigeid peaks nõustama esmatasandi meditsiinitöötajad (2C).
*Nõustamisel peab arvestama KNH raskusatet, riskitegureid ja sotsiaalset tausta.
*Varajase KNHga diabeeti põdevaid patsiente peab nõustama VR, VS, kolesterooli jälgimise osas, et aeglustada haiguse progressiooni (2C).
*Diabeediga haigeid peab nõustama regulaarse (igapäevase) füüsilise aktiivsuse osas (2D).

Table 40 | GRADE system for grading quality of evidence

Step 1: Starting grade for quality of evidence based on study design	Step 2: Reduce grade	Step 3: Raise grade	Final grade for quality of evidence and definition
Randomized trials = High	*Study quality* -1 level if serious limitations -2 levels if very serious limitations *Consistency* -1 level if important inconsistency	*Strength of association* +1 level is strong[a], no plausible confounders +2 levels if very strong[b], no major threats to validity *Other* +1 level if evidence of a dose-response gradient +1 level if all residual plausible confounders would have reduced the observed effect	High = Further research is unlikely to change confidence in the estimate of the effect Moderate = Further research is likely to have an important impact on confidence in the estimate of effect, and may change the estimate
Observational study = Low	*Directness* -1 level if some uncertainty -2 levels if major uncertainty		Low = Further research is very likely to have an important impact on confidence in the estimate and may change the estimate
Any other evidence = Very low	*Other:* -1 level if sparse or imprecise data[c] -1 level if high probability of reporting bias		Very low = Any estimate of effect is very uncertain

Abbreviation: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.
[a]Strong evidence of association is defined as 'significant relative risk of >2 (<0.5)' based on consistent evidence from two or more observational studies, with no plausible confounders.
[b]Very strong evidence of association is defined as 'significant relative risk of >5 (<0.2)' based on direct evidence with no major threats to validity.
[c]Sparse if there was only one study or if the results include just a few events or observations and were uninformative. Imprecise if the confidence interval spans a range greater than 1 or confidence limits are <0.5 to >2.0
Adapted by permission from Macmillan Publishers Ltd: *Kidney International*. Uhlig K, Macleod A, Craig J et al.[725] Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2006; 70: 2058–2065; accessed http://www.nature.com/ki/journal/v70/n12/pdf/5001875a.pdf

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.

KHA_CARI (Modification of lifestyle and nutrition interventions for management of early chronic kidney disease)

*Progresseeruva KNHga haiged peaks saama dieedialast nõustamist dietoloogi käest (2C).
*Varajase KNHga patsientidele on soovitav normaalse valgusisaldusega dieet (0,75-1,0 g/kg/päevas) (1C).
*Madala valgusisaldusega dieet (<=0.6 g/kg/päevas) pole soovituslik KNH süvenemise aeglustamiseks alatoitumuse riski tõttu.
*Suurema valgu sisaldusega dieedi korral on soovitav valgu tarbimist vähendada vastavalt RDI soovitustele (2C).
*Soovitav vähendada naatriumi tarbimist kuni 100 mmol/päevas (või 2.3 g naatriumi või 6 g soola päevas) või vähem. See alandab VR ja proteinuuriat KNHga patsientidel. (1C).
*Varajase KNHga patsiendid ei pea vähendama fosfori tarbimist kuna see ei halvenda ei KNH ega südame-veresoonkonna haiguste prognoosi (2C).
*Hüperkaleemiaga patsiendid peavad vähendama kaaliumi tarbimist, dieedi osas peab neid nõustama dietoloog (2C).
*Ülekaalulistel on soovitav langetada kehakaalu, see võib parandada KNH prognoosi (1C).
*Soovitav KMI 18,5-24,9 kg/m2, vöö ümbermõõt meestel <= 102cm, naistel <= 88cm.
*Soovitav süüa puu- ja juurvilju, see alandab VR. (2D)
*Soovitav kiudainete rikas dieet, vähendab põletikulist aktiivsust, vähendab suremust KNHga patsientidel. (2D)
*Varajase staadiumi KHNga patsientidel vedeliku tarbimine 2-2,5l/päevas (koos toidus sisalduva vedelikuga).

SIGN

*Soovitab nõustada KNH patsiente suitsetamisest loobumisel ja ülekaalu vähendamisel.
*Soovitatakse KNH patsientidel vähendada soolatarvitamist, tegeleda regulaarse füüsilise koormusega, loobuda suitsetamisest ja järgida tervislikke eluviise.
*Valgu piiramine (<0,8g/kg/day) 1-3 raskusastme haigetel pole näidustatud.
*Hüpertoonia ja KNH 1.-4. raskusastmega patsientidele soovituslik piirata naatriumi tarbimist *(<2.4 g/päevs või <100 mmol/päevas või <6 g soola)* et alandada VR ja vähendada südame-veresoonkonna haiguste riski.
*Kui KNHga patsientidel on vöö ümbermõõt meestel >=94cm ja naistel >=80cm on näidustatud kehakaalu langetamine. Sellega peaks tegelema spetsialist (dietoloog).
*KNHga patsientidel on näidustatud regulaarne füüsiline aktiivsus.

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review, or RCT rated as 1^{++}, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}

Kokkuvõte:

Üldine info:
*Esmatasandi meditsiinitöötajad peavad nõustama riskirühma ja KNH haigeid (2C). Nõustamisel peab arvestama KNH raskusastme, riskitegurite ja sotsiaalse taustaga. Varajase KNH raskusastme diabeeti põdevaid inimesi peab nõustama VR, VS, kolesterooli jälgimise osas, et aeglustada haiguse progresseerumist (2C). KHA-CARI

Kehakaal:
*Nii riskirühma kui varajase KNHga patsiente on vaja nõustada dieedi ja elustiili osas. KHA-CARI
*Kehakaalu jälgimine, regulaarne füüsiline aktiivsus, tervislik toitumine ja mitte suitsetamine on kasulik kõigile ja eriti oluline inimestel, kellel on südame-veresoonkonna haigused. NICE
*Soovitab jälgida kehakaalu, soovituslik normkaalust kõikumine 5% ulatuses. Normkaaluga on väiksem tõenäosus haigestuda KNHsse (2C). KHA-CARI
*Kaalu langetamiseks farmakoloogiliste preparaatide kasutamine kombinatsioonis mitte medikamentoossete meetoditega langetab riski haigestuda KNHsse (2B). KHA-CARI
*Ülekaalulistel on soovitav langetada kehakaalu, see võib parandada KNH prognoosi (1C). KHA-CARI
*Soovitav KMI 18,5-24,9 kg/m2, vöö ümbermõõt meestel <= 102cm, naistel <= 88cm. KHA-CARI
*Oluline jälgida kehakaalu, vajadusel nõustada kehakaalu langetamisel. SIGN
*Kui KNHga patsientidel vöö ümbermõõt meestel >=94cm ja naistel >=80cm on näidustatud kehakaalu langetamine. Sellega peaks tegelema spetsialist (dietoloog). SIGN

Füüsiline aktiivsus:
*Regulaarne füüsiline aktiivsus peab olema sobiv arvestades patsiendi füüsilist vormi, võimeid ja haiguse anamneesi. KHA-CARI
*Diabeediga haigeid peab nõustama regulaarse (igapäevase) füüsilise aktiivsuse osas (2D). KHA-CARI
*KNHga inimestel on näidustatud regulaarne füüsiline aktiivsus. SIGN

Suitsetamine ja alkohol:
*Puudusid tõendid selle kohta, kas inimestel kellel on krooniline neeruhaigus ja kes suitsetavad on veelgi suurem risk haigestuda südame-veresoonkonna haigustesse, võrreldes inimestega, ilma kroonilise neeruhaiguseta. KHA-CARI
*Suitsetamisest loobumisel ja alkoholi liigtarbimisel pakkuda psühholoogilist abi. KHA-CARI
*Alkoholi tarbimise mõju kohta KNH patsientidel on uuringutes olnud erinevad tulemused ja ei ole otseseid tõendeid alkoholi mõjust KNH progresseerumisele, kuid KNH patsientidel on mõistlik alkoholi tarbimist vähendada. Malaysia_CKD
*Puudusid tõendid kahjulike mõjude kohta alkoholi tarbimisel haigestumisel KNHsse. NICE
*Soovitatakse KNH patsientidel vähendada soolatarbimist, tegeleda regulaarse füüsilise koormusega, loobuda suitsetamisest ja järgida tervislikke eluviise. SIGN

Vererõhk:
*Riskirühma ja 1.-2. KNH raskusastme haigetel vererõhu kontroll 1 x aastas, soovituslikult saada VR <140/90 mmHg tasemele (1A). KHA-CARI
*Diabeeti põdevatel patsientidel soovitav jälgida VR väärtusi ka kodus (1C). KHA-CARI
*Patsientidel KNH raskusatmes 3a., 3b VR kontroll iga 3-6 kuu tagant. KHA-CARI

Naatrium:
*Madala soolasisaldusega dieet (2,3 g/päevas) langetab haigestumise riski (2C). KHA-CARI
*KNHga patsientidel on soovitav vähendada naatriumi tarbimist kuni 100 mmol/päevas (või 2.3 g naatriumi või 6 g soola päevas) või vähem. See alandab VR ja proteinuuriat KNHga patsientidel. (1C). KHA-CARI
*Naatriumi piiramist tuleks KNHga patsientidel alustada 2,4 g/päevas, sest Na+ tarbimine on otseses seoses albuminuuria süvenemisega. Malaysia_CKD
*Hüpertoonia ja KNH 1.-4. raskusastmega patsientidele soovituslik piirata naatriumi tarbimist *(<2.4 g/päevs või <100 mmol/päevas või <6 g soola)* et alandada VR ja vähendada südame-veresoonkonna haiguste riski. SIGN

Valk:
*KNH riskirühmas valgu tarbimise suhteline kasu vs kahju ei ole piisavalt tõestatud (2D). KHA_CARI
*3.-5. KNH raskusastme patsientidel on soovituslik valgu piiramine toidus 0,6-0,8 g/kg/päevas ja piisava energia tarbimine päevas 30-35 kcal/kg/päevas. Valgu piiramist peab jälgima dietoloog. (Grade B). Valgu piiramine väljendunud mikroalbuminuuria ja proteinuuria puhul 0,8-1,0 g/kg/päevas. Malaysia_CKD
*Vähese valgusisaldusega dieeti ei soovitata kõikidele KNH patsientidele, peab vaatama vanust, eGFRi, diabeeti jm. tegureid. Uuringutes on leitud seos KNH progresseerumise ja suitsetamise vahel, ka peale kohandamist diabeediga. NICE
*Valgu piiramine (<0,8g/kg/day) 1-3 raskusastmega KNH patsientidel ei ole näidustatud. SIGN
*Progresseeruva KNH haiged peavad saama dieedialast nõustamist dietoloogi käest (2C). KHA-CARI
*Varajase KNH patsientidele on soovitav normaalse valgusisaldusega dieet (0,75-1,0 g/kg/päevas) (1C). KHA-CARI
*Madala valgusisaldusega dieet (<=0.6 g/kg/päevas) pole soovituslik KNH süvenemise aeglustamiseks alatoitumuse riski tõttu. KHA-CARI
*Suurema valgu sisaldusega dieedi korral on soovitav valgu tarbimist vähendada vastavalt RDI (Reference Daily Intake) soovitustele (2C). KHA-KARI

Kaalium:
*Hüperkaleemiaga patsiendid peavad vähendama kaaliumi tarbimist, dieedi osas peab neid nõustama dietoloog (2C).
Fosfor:
*Varajase KNHga patsiendid ei pea vähendama fosfori tarbimist kuna see ei halvenda ei KNH ega südame-veresoonkonna haiguste prognoosi (2C). KHA-CARI

Veel dieedist:
*Toitumissoovitustes jälgida kaaliumi, fosfori, kalorite ja soola tarvitamist. Pakkuda toitumissoovitusi kaaliumi, fosforit, kalorite ja soola tarvitamises. Kaaliumi, fosfori, kalorite ja soola tarvitamist peaks jälgima toitumisspetsialist. NICE
*Soovitavon süüa puu- ja juurvilju, see alandab VR. Soovitav kiudaineterikas dieet, vähendab põletikulist aktiivsust, vähendab suremust KNHga patsientidel (2D). KHA-CARI
*Varase staadiumi KHNga patsientidele on soovituslik vedeliku tarbimine 2-2,5 l/päevas (koos toidus sisalduva vedelikuga). KHA-CARI