

Neues und Altes – neu gedacht – zur chronischen Nierenerkrankung CKD

Anlässlich des Satellitensymposiums am Weltnierentag

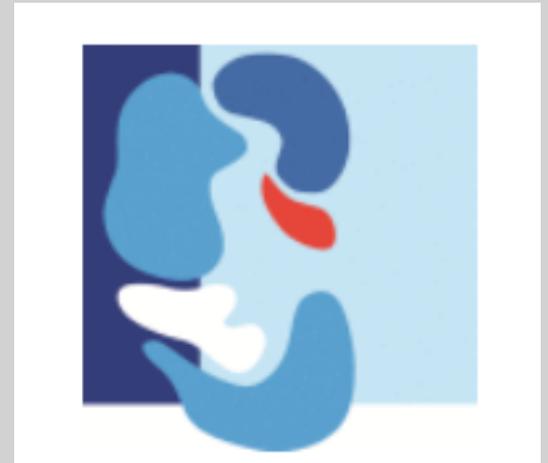
Dr. med. Alexandra Günther

Nephrologie SRRWS und Nierenzentrum Rheintal

labormedizinisches zentrum
centre des laboratoires médicaux
centro medicina di laboratorio

Dr Risch 

XXV. Diagnostik-Symposium
14.03.2019, Schaan



Nierenzentrum Rheintal

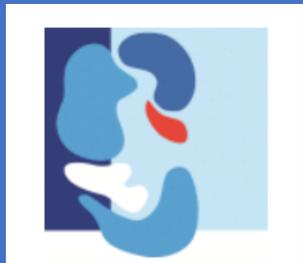
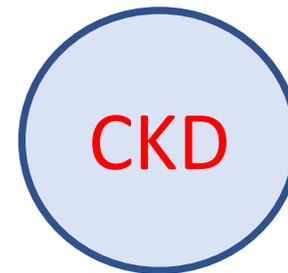
 **SPITALREGION**
RHEINTAL
WERDENBERG
SARGANSERLAND

Chronische Nierenerkrankung (CKD)

GFR <60ml/min normiert auf 1,73m²

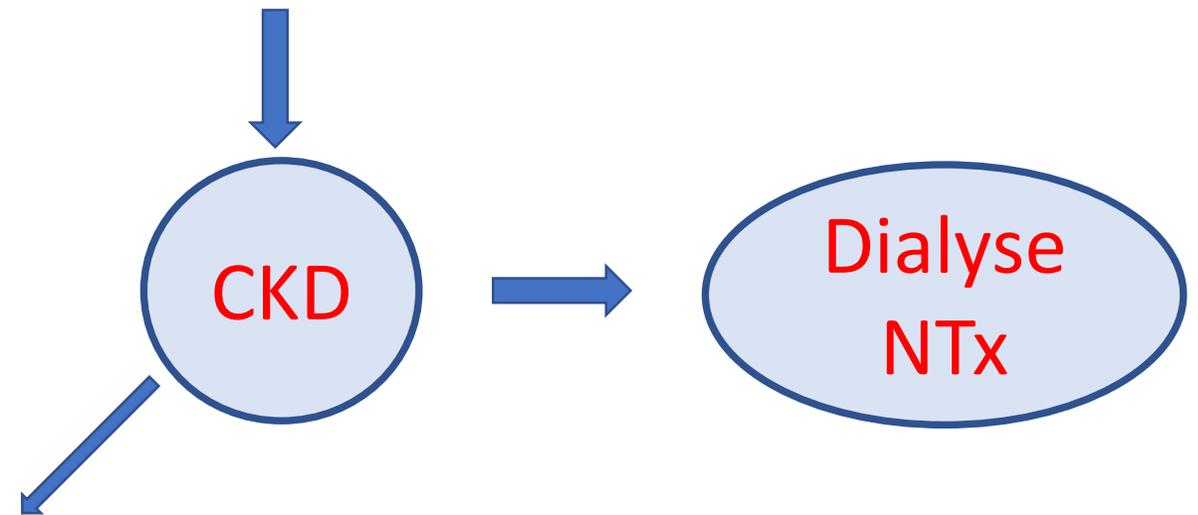
und / oder

morphologische Zeichen einer Nierenerkrankung



Chronische Nierenerkrankung (CKD)

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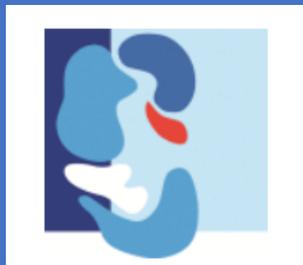


Epidemiologie: 10-15% !

Häufiger als Diabetes (= 9,9% in 2010)!

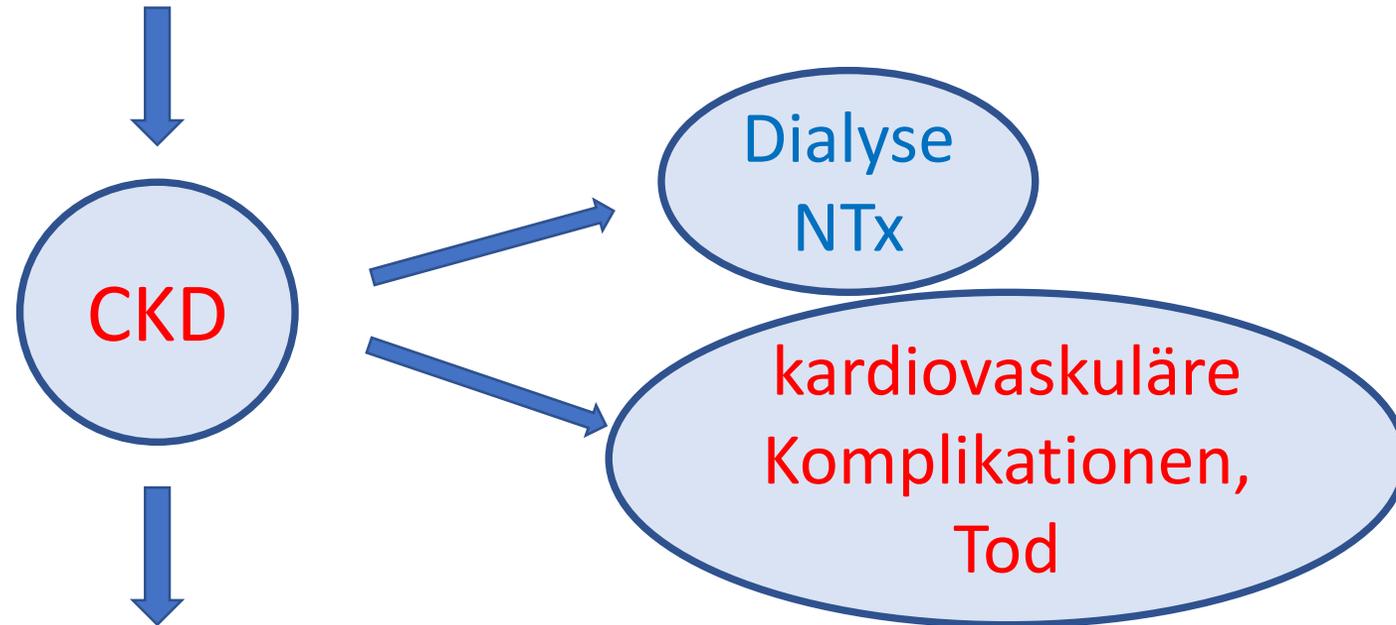
Prävalenz und Inzidenz von Diabetes mellitus in Deutschland Dtsch Arztebl Int 2016; 113(11): 177-82

(65 Millionen Versichertendaten der gesetzlichen Krankenkassen aus den Jahren 2009 und 2010)

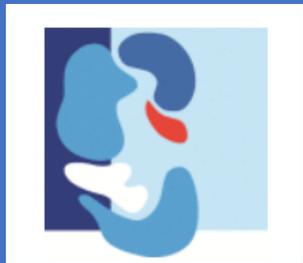


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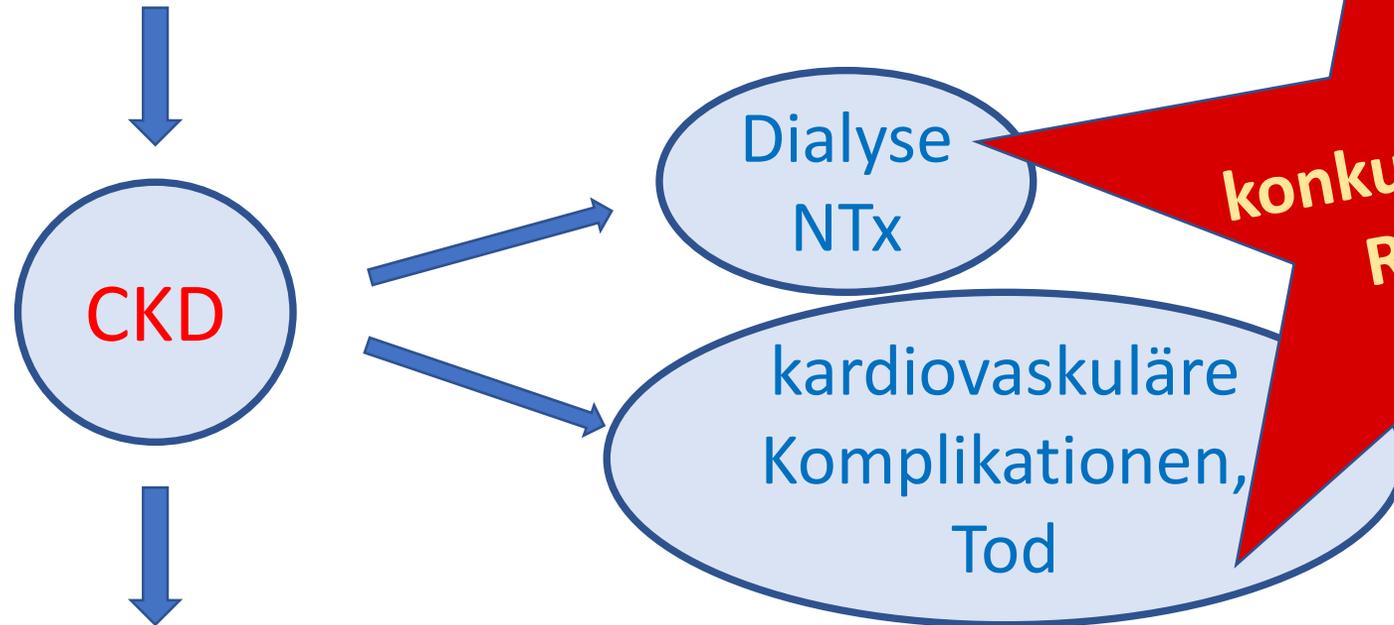


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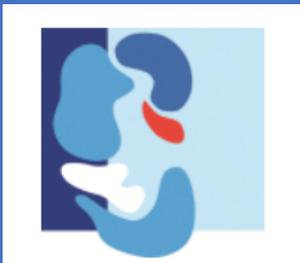
Chronische Nierenerkrankung (CKD)

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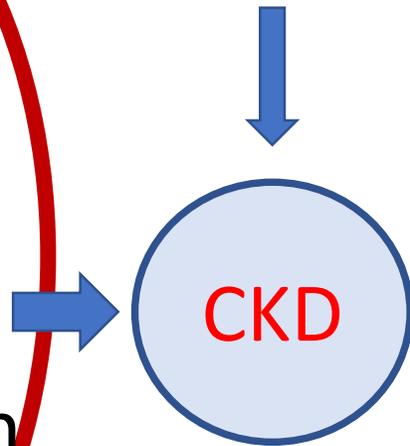
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Dialysepatienten = „Survivors“



Chronische Nierenerkrankung (CKD)

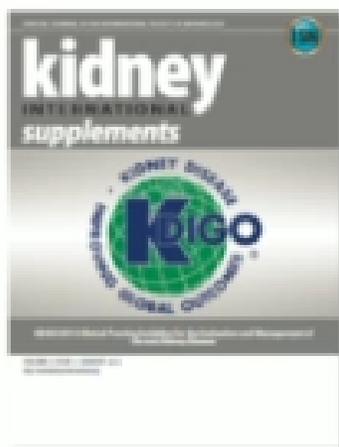
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Epidemiologie: 10-15% !



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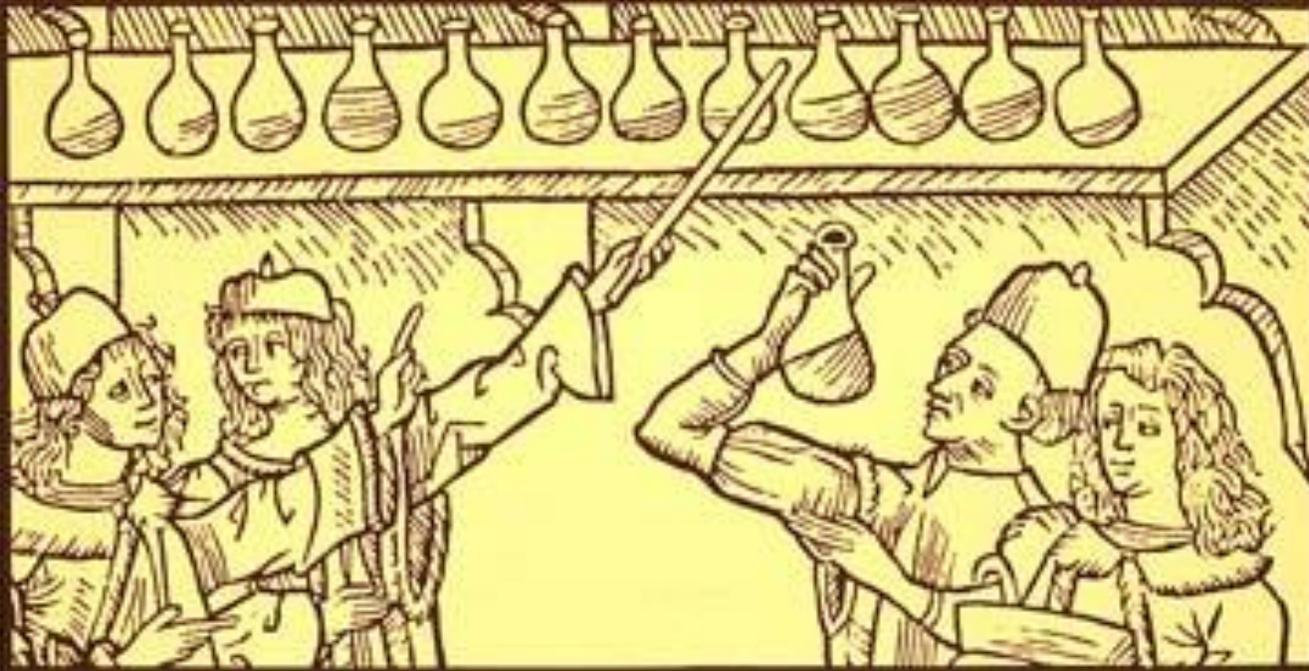


**Prognosis of CKD by GFR
and Albuminuria Categories:
KDIGO 2012**

			Persistent albuminuria categories Description and range			
			A1	A2	A3	
			Normal to mildly increased	Moderately increased	Severely increased	
			<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol	
GFR categories (ml/min/1.73m ²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Figure 9 | Prognosis of CKD by GFR and albuminuria category. Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes. Modified with permission from Macmillan Publishers Ltd: *Kidney International*. Levey AS, de Jong PE, Coresh J, et al.³⁰ The definition, classification, and prognosis of chronic kidney disease: a KDIGO controversies conference report. *Kidney Int* 2011; 80: 17-28; accessed <http://www.nature.com/ki/journal/v80/n1/full/ki2010483a.html>





Prinzip :
lieber gut geschätzt als
schlecht gemessen

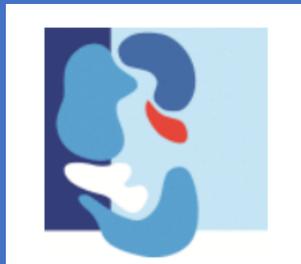
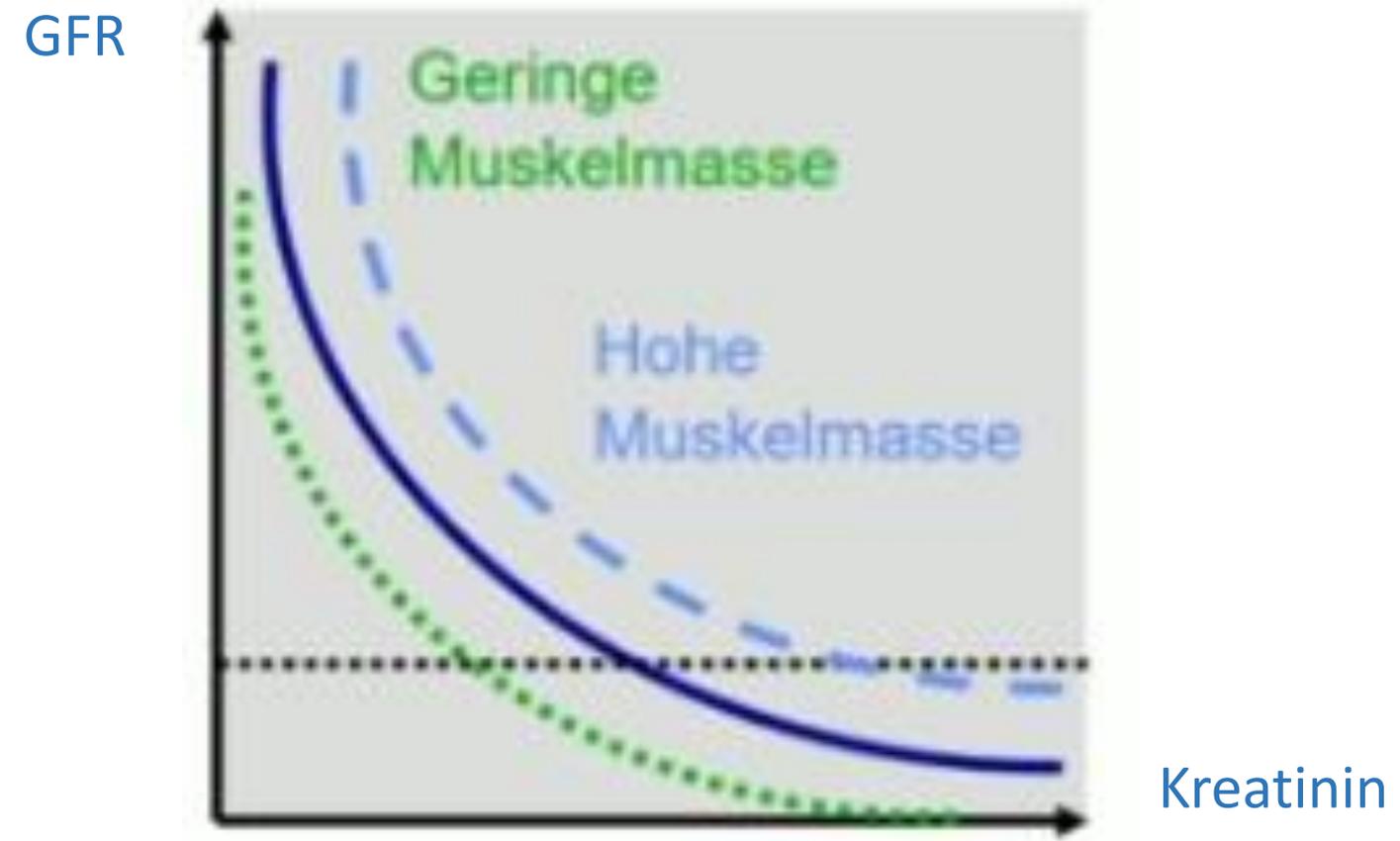
- Albuminurie bzw. Proteinurie:
- normal: <math><30 \text{ mg/g Krea}</math> (<math>< 3 \text{ mg/mmol Krea}</math>)
- Albuminurie: $30 - 300 \text{ mg/g Krea}$ ($3 - 30 \text{ mg/mmol Krea}$)
- Albuminurie: $> 300 \text{ mg/g Krea}$ ($>30 \text{ mg/mmol Krea}$)

• "Große oder nephrotische Proteinurie": $> 3000 \text{ mg/g Krea}$ (oder auch in g/g Krea angegeben)

Teilweise wird die Einheit **mg/mmol Krea** verwendet, Umrechnungsfaktor für Kreatinin: $1 \text{ g} = 8,8417 \text{ mmol}$
Überschlägig betragen die Werte dann ein Zehntel gegenüber der Angabe in mg/g Krea.

Frauen 0,5 – 1,3 g Urin-Krea /die
Männer 1,2 – 2,5 g Urin-Krea/die!!

Kreatinin als endogener Filtrationsmarker ist Abhängig von der Muskelmasse

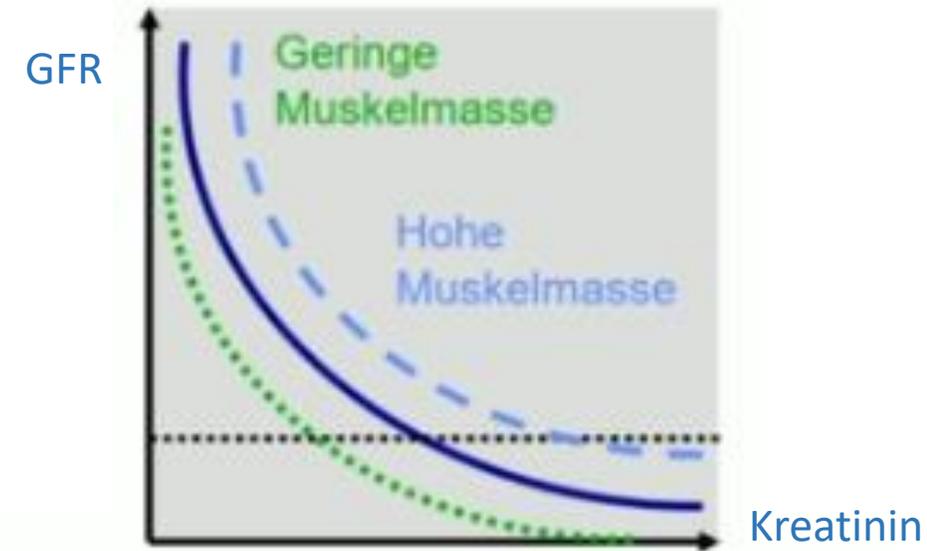


Originalarbeit 1973 zu
Cockroft-Gault Formel mit
n=249 , veraltet

Originalarbeit 1999
n=1628 zur Ermittlung der
MDRD-Formel, sie
unterschätzt oft die GFR

Cockroft-Gault und MDRD
sind in hohen GFR-
Bereichen weniger genau

CKD-EPI: 2012 mit >8000
Probanden und >4000
Kontrollen entwickelt,
2017 revidiert
(<http://nierenrechner.de/index.php?page=egfr-ckd-rechner>)



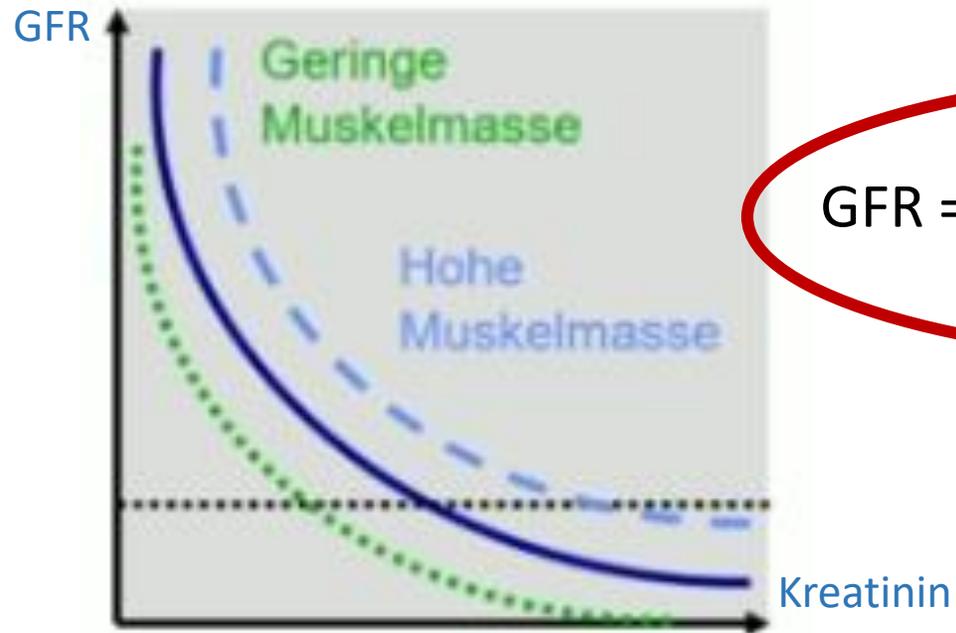
Konzept der „estimated GFR“ (eGFR)

Cockroft - Gault
$$\frac{(140 - \text{Alter}) \times \text{KG (kg)}}{[\text{Krea}] \text{ S} \times 72} \times 0,85 \text{ für Frauen}$$

MDRD IV
$$[\text{Krea}] \text{ S} \times 186^{-1,154} \times \text{Alter}^{-0,203} \times 0,74 \text{ für Frauen}$$

CKD EPI
$$144 \times \min [\text{Krea}] \text{ S} / (0,7-0,329 \text{ oder } 1,209) \times 0,993 \times \text{Alter} \text{ für Frauen}$$

$$141 \times \min [\text{Krea}] \text{ S} / (0,9-0,411 \text{ oder } 1,209) \times 0,993 \times \text{Alter} \text{ für Männer}$$



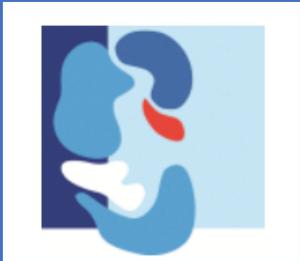
GFR = Anzahl Glomeruli + SNGFR

Konzept der „estimated GFR“ (eGFR)

Cockroft - Gault $\frac{(140 - \text{Alter}) \times \text{KG (kg)}}{[\text{Krea}] \text{ S} \times 72} \times 0,85$ für Frauen

MDRD IV $[\text{Krea}] \text{ S} \times 186^{-1,154} \times \text{Alter}^{-0,203} \times 0,74$ für Frauen

CKD EPI
 144 x min $[\text{Krea}] \text{ S} / (0,7-0,329 \text{ oder } 1,209) \times 0,993 \times \text{Alter}$ für Frauen
 141 x min $[\text{Krea}] \text{ S} / (0,9-0,411 \text{ oder } 1,209) \times 0,993 \times \text{Alter}$ für Männer



ORIGINAL ARTICLE

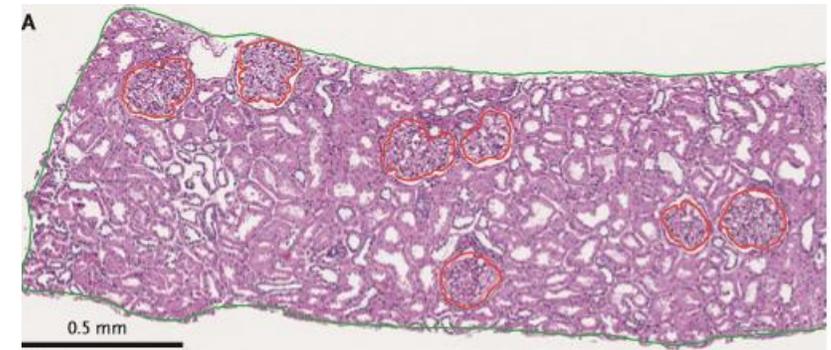
Single-Nephron Glomerular Filtration Rate in Healthy Adults

Aleksandar Denic, M.D., Ph.D., Jerry Mathew, M.D.,
Lilach O. Lerman, M.D., Ph.D., John C. Lieske, M.D., Joseph J. Larson, B.S.,
Mariam P. Alexander, M.D., Emilio Poggio, M.D., Richard J. Glassock, M.D.,
and Andrew D. Rule, M.D.

A: kortikales Volumen im CT

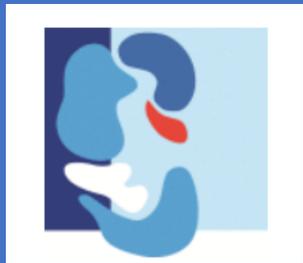


B. „0-Biopsie“: Dichte von sklerotischen
und nicht-sklerotischen Glomeruli



C: GFR

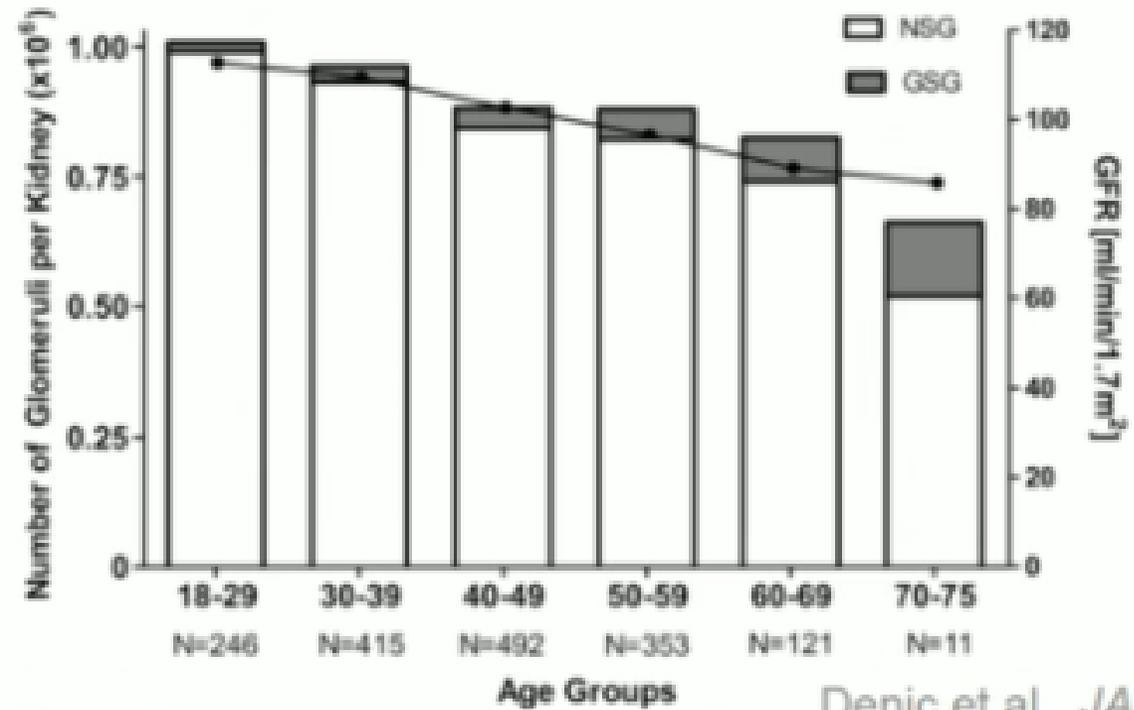
N ENGL J MED 376;24 nejm.org June 15, 2017



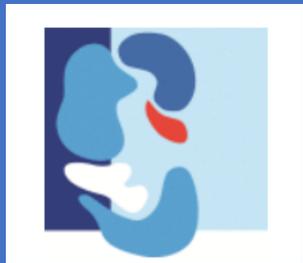
Anzahl intakter und sklerotischer Glomeruli

Denic et al. JASN 2017

Gesamtzahl von
sklerotischen
(GSG)
und intakten
Glomeruli (NSG)



Denic et al., JASN 2017



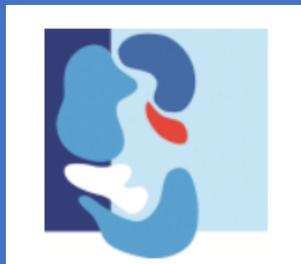
ORIGINAL ARTICLE

Single-Nephron Glomerular Filtration Rate
in Healthy Adults**Table 2.** Age-Group Differences in the Number of Nephrons per Kidney, the Single-Nephron GFR, and Total GFR among 1388 Living Kidney Donors.

Age Group	No. of Donors	No. of Nephrons	Single-Nephron GFR	Total GFR
			<i>nl/min</i>	<i>ml/min</i>
18–29 yr	190	970,000±430,000	79±42	127±25
30–39 yr	339	930,000±350,000	77±36	124±24
40–49 yr	417	850,000±360,000	81±42	114±23
50–59 yr	300	810,000±360,000	80±40	106±20
60–64 yr	73	750,000±310,000	79±36	101±18
65–69 yr	56	720,000±260,000	76±33	95±17
70–75 yr	13	480,000±170,000	110±44	96±25

Nephrene: 860.000 +- 370.000 / Niere

SNGFR: 80 +- 40 nl/min: sehr konstant



Single-Nephron Glomerular Filtration Rate in Healthy Adults

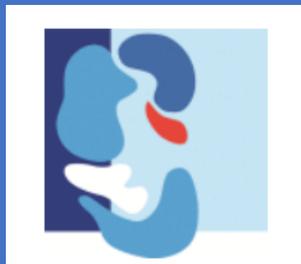
Table 3. Demographic and Clinical Characteristics as Predictors of the Number of Nephrons per Kidney, Single-Nephron GFR, and Total GFR.*

Characteristic	No. of Nephrons		Single-Nephron GFR		Total GFR	
	Estimate	P Value	Estimate <i>nl/min</i>	P Value	Estimate <i>ml/min</i>	P Value
Age, per 10 yr	-60,000	<0.001	1	0.28	-7.1	<0.001
Female sex	-60,000	0.03	6	0.08	-3.8	0.01
Body-mass index, per SD	0	0.85	6	<0.001	9.6	<0.001
Height, per SD†	30,000	0.03	4	0.006	9.2	<0.001
Uric acid, per SD	-40,000	0.002	1	0.42	-3.7	<0.001
Family history of end-stage renal disease	-70,000	<0.001	8	<0.001	0.8	0.43
Mild hypertension	-20,000	0.59	3	0.39	1.5	0.36

* The estimate is the difference with the presence of the characteristic versus its absence (female sex vs. male sex; presence vs. absence of family history of end-stage renal disease; and mild hypertension vs. no hypertension) or with the level increase of the characteristic (for age, body-mass index, height, and uric acid level). The standard deviation (SD) was 4.9 for body-mass index, 9.5 cm for height, and 1.4 mg per deciliter (80 μ mol per liter) for uric acid. The analysis was adjusted for each of the other demographic or clinical characteristics in the 1388 donors.

† Statistical significance for the single-nephron GFR was influenced by donors with a height of more than 190 cm.

SNGFR: nicht abhängig von Alter (<70 J), Geschlecht, Grösse, (< 190cm)



Single-Nephron Glomerular Filtration Rate in Healthy Adults

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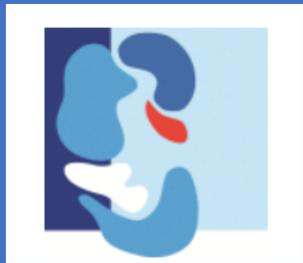
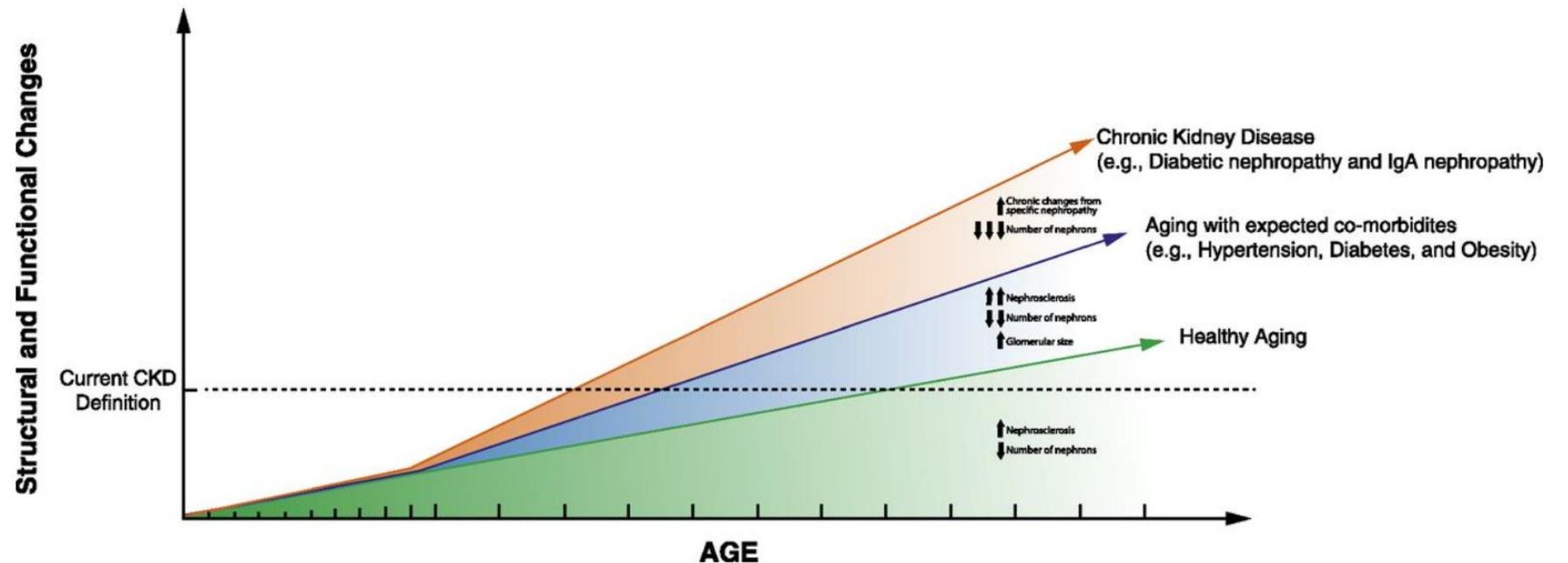
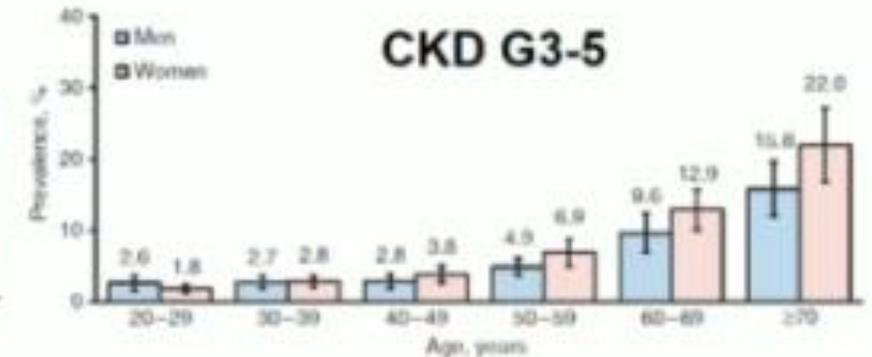
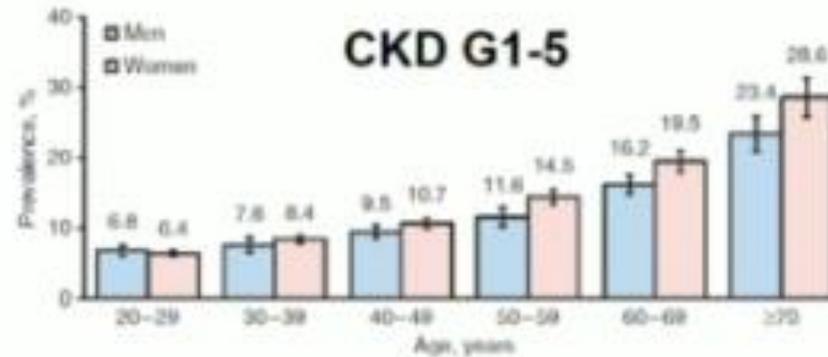
SNGFR: nicht abhängig von Alter (<70 J), Geschlecht, Grösse, (< 190cm)
aber:

höhere SNGFR assoziiert mit vergrößerten Glomeruli, Glomerulosklerose
Risikofaktoren für CKD (fam. Belastung, Übergewicht) = Hyperfiltration



Altersabhängigkeit von CKD

- 10–15 % der Bevölkerung



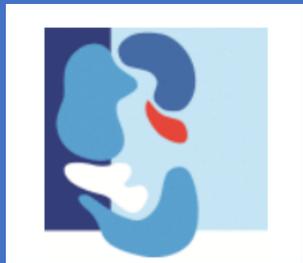
ORIGINAL ARTICLE

History of Childhood Kidney Disease and Risk of Adult End-Stage Renal Disease

Ronit Calderon-Margalit, M.D., M.P.H., Eliezer Golan, M.D., Gilad Twig, M.D., Ph.D.,
Adi Leiba, M.D., Dorit Tzur, M.B.A., Arnon Afek, M.D., M.P.H.,
Karl Skorecki, M.D., and Asaf Vivante, M.D., Ph.D.

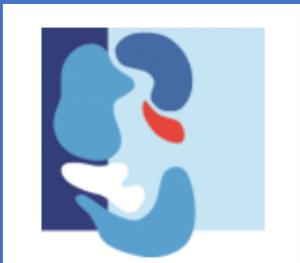
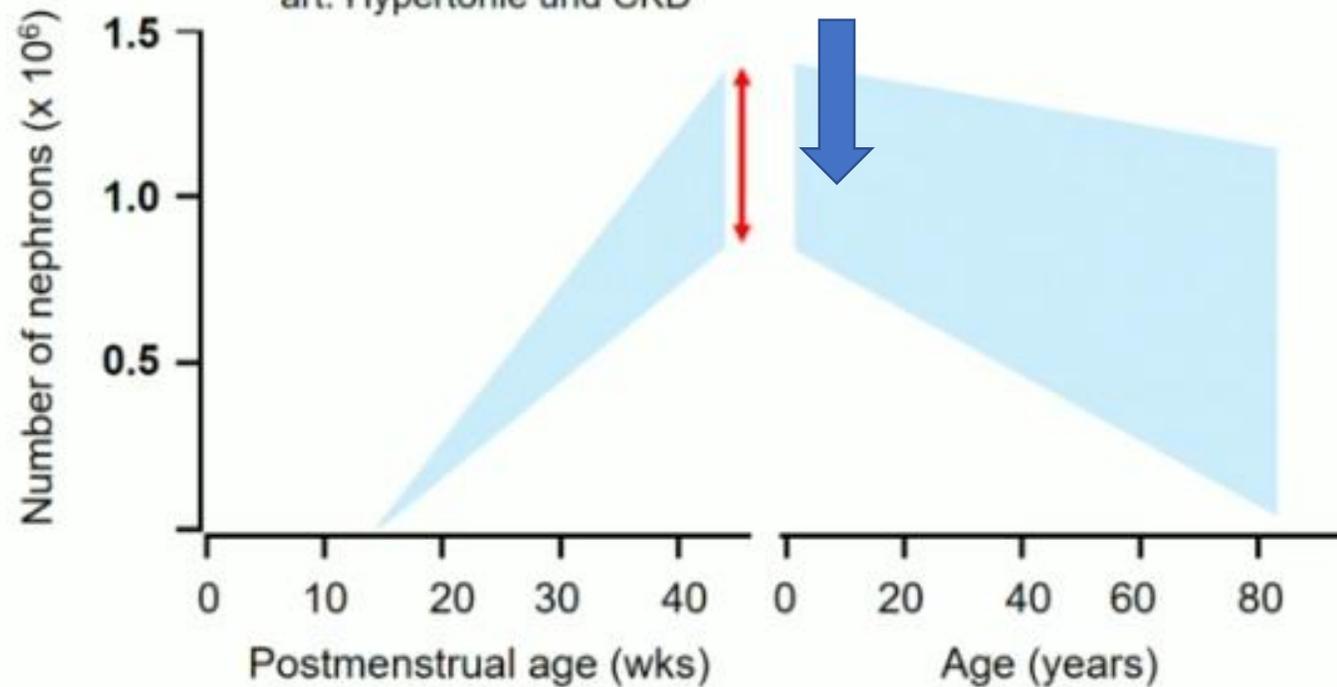
Israelische Studie:
Musterung zum Militär und Langzeit-Follow up
in Abhängigkeit von St.n. Nierenproblemen in der Kindheit

→ Erhöhung der CKD-Rate in diesem Kollektiv



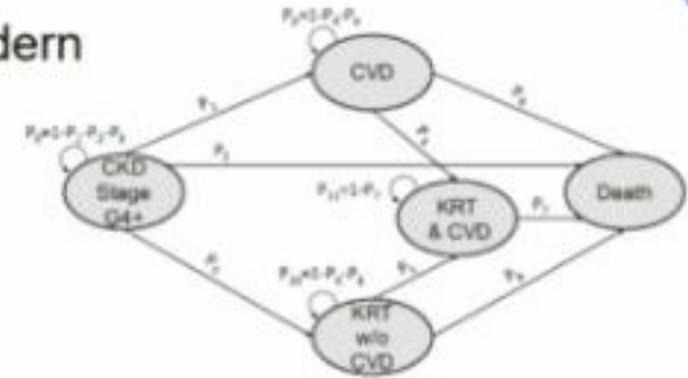
Nach Ereignis im Kindesalter

- Intrauterine Entwicklung bestimmt Nephronzahl
- Je weniger Nephrone, desto höher das Risiko für art. Hypertonie und CKD



Prognose von Patienten mit CKD G4 +

Metaanalyse; N=294.296 aus 30 Ländern



<http://www.kdigo.org/equation/>

Age (30-85 yr) **60**

Sex **Male**

RACE (white or black) **White**

eGFR (ml/min per 1.73 m²) **25**

Systolic Blood Pressure (mm Hg) **140**

History of Cardiovascular Disease **Yes**

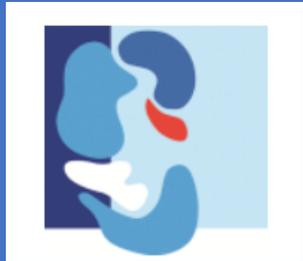
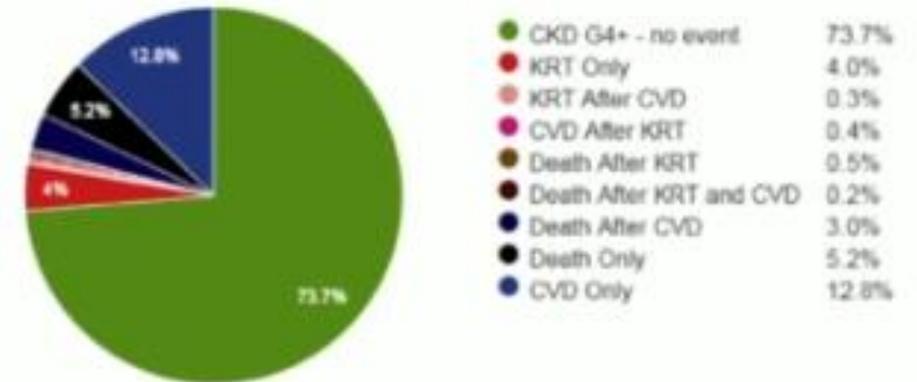
Diabetes **No Diabetes**

Urine Albumin to Creatinine (mg/g) **30**

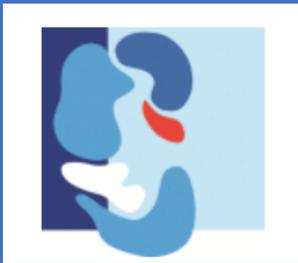
Smoking History **Not Current Smoker**

Risk at 2 Years

Outcome	Risk
Any Kidney Replacement Therapy (KRT a.k.a. ESRD)	5.3%
Any Cardiovascular Disease (CVD)	16.6%
Any Death	8.9%

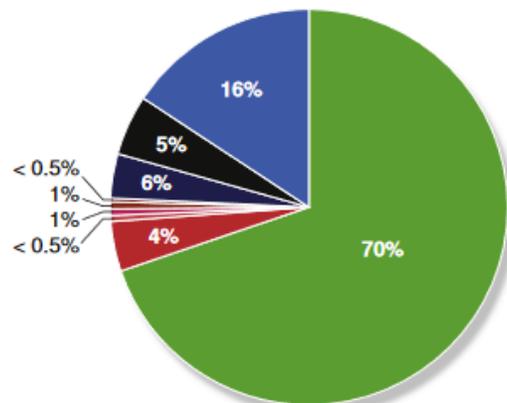


Grams et al., *Kidney Int* 2018; Eckardt et al. *Kidney Int* 2018



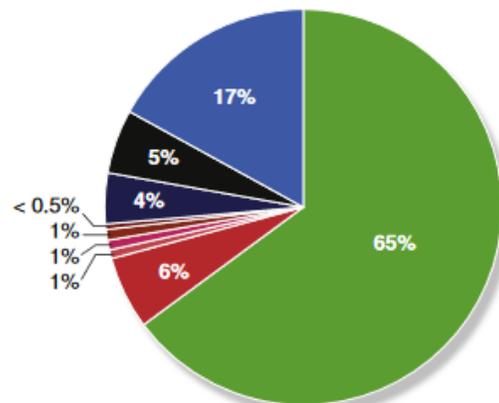
SPITALREGION
RHEINTAL
WERDENBERG
SARGANSERLAND

2 year ACR 30



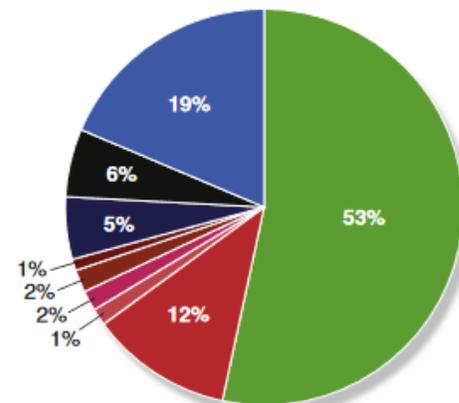
6% any KRT
12% death

2 year ACR 100



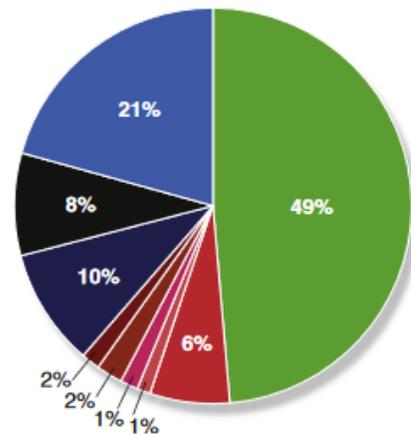
9% any KRT
11% death

2 year ACR 1000



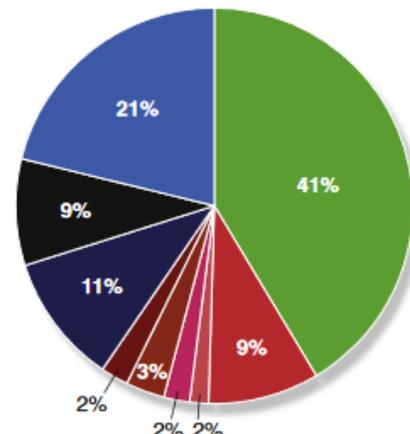
17% any KRT
13% death

4 year ACR 30



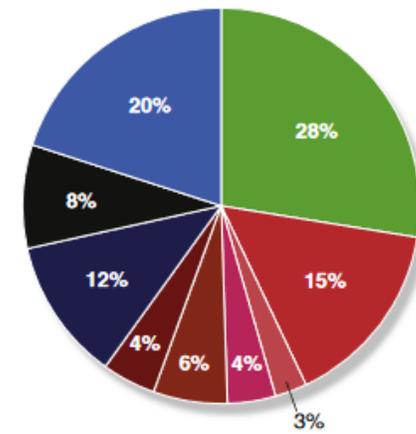
13% any KRT
22% death

4 year ACR 100

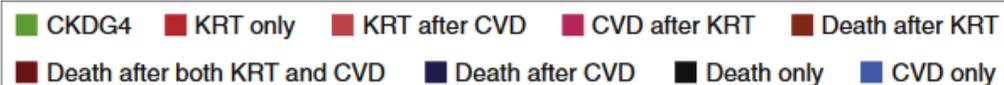


18% any KRT
25% death

4 year ACR 1000



32% any KRT
30% death



<http://www.kdigo.org/equation/> Grams et al.
Kidney Int 2018; Eckardt et al. *Kidney Int* 2018

www.kidney-international.org

KDIGO executive conclusions



Improving the prognosis of patients with severely decreased glomerular filtration rate (CKD G4+): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

see related clinical investigation on page 1442

OPEN

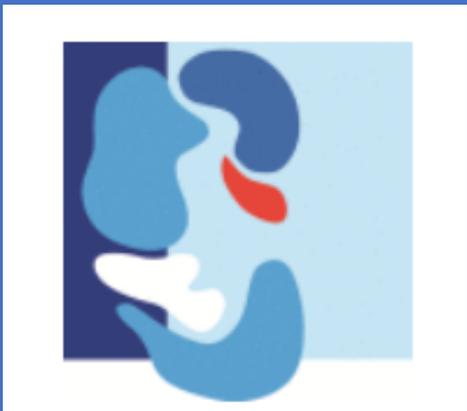
Kai-Uwe Eckardt¹, Nisha Bansal², Josef Coresh³, Marie Evans^{4,5}, Morgan E. Grams^{3,6}, Charles A. Herzog^{7,8}, Matthew T. James^{9,10}, Hiddo J.L. Heerspink¹¹, Carol A. Pollock^{12,13}, Paul E. Stevens¹⁴, Manjula Kurella Tamura^{15,16}, Marcello A. Tonelli⁹, David C. Wheeler¹⁷, Wolfgang C. Winkelmayer¹⁸, Michael Cheung¹⁹ and Brenda R. Hemmelgarn^{9,10}, for Conference Participants²⁰



zusammenfassende Ermunterung:

- Messen Sie Kreatinin /GFR und schauen Sie sich den Patienten an
- Machen Sie Urinstix
- Schauen Sie dort auf Albuminurie und Hämaturie
- Merken Sie sich die magische Zahl 60ml/min und bedenken Sie die Risikokonstellation
- Messen Sie den Blutdruck
- Verhindern Sie Hyperfiltration
- Geben Sie RAAS Blocker, behandeln Sie DM und HTN

Neues und
Altes – neu gedacht –
zur chronischen
Nierenerkrankung
CKD



 **SPITALREGION**
RHEINTAL
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labormedizinisches zentrum
centre des laboratoires médicaux
centro medicina di laboratorio

Dr Risch 

Satellitensymposium am
Weltnierentag
zum
XXV. Diagnostik-Symposium
14.03.2019, Schaan

Vielen Dank! – Merci !