بنام آنکه هستی نام از او یافت
فلک جنبش زمین آرام از او یافت

The 19th International Congress of Nephrology, Dialysis and Transplantation (ICNDT)

12-15 December 2023
Homa Hotel, Tehran

Supplements and the kidney

Is it body building or kidney damaging?

Dr. Mohammad Tamaddondar

Nephrologist

Hormozgan university of medical science

TEHRAN 2023

Home message

- ✓Creatine use seems not affect kidney function(in recommended dose)
- ✓High protein diet specially animal type is harmful
- ✓Anabolic androgenic steroids is banned
- ✓High dose vitamins not recommended

Bodybuilding

The use of progressive resistance exercise to develop muscle building by hypertrophy

Appearances of muscular definition and symmetry (rather than athletic ability).

- ✓Over 95% of bodybuilders use dietary supplements, with the two most common being creatine monohydrate and protein

- ✓Non-nutritional, performance-enhancing drugs, such as veterinary-grade vitamin supplementation, and/or anabolic–androgenic steroids (AAS),Growth Hormone (GH)are also used .

Most of the extreme nutritional, drug and training strategies in bodybuilding are from non-evidence-based sources,

and potential adverse health impact effect are possible.

1-Which organ doesn’t play role in creatine production ?

a-liver

b-kidney

c-pancreas

d-muscle

2-Which protein doesn't increase GFR?

a-white egg

b-fish

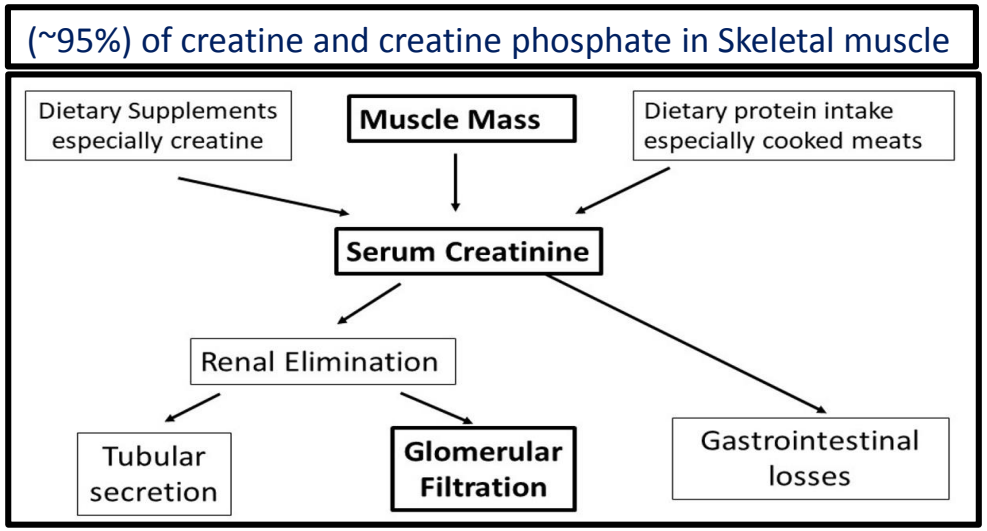
c-soy

d-beef

OBJECTS

- ✓Creatine
- ✓Protein
- ✓Anabolic androgenic steroids /GH
- ✓vitamins

Assessment of kidney function
presence of unrecognized CKD



Cystatin C

Is not related to muscle mass and diet.

Cystatin C based MDRD eGFR measuring

Increased when using anabolic androgen steroid (AAs)

Assessment of Dietary Protein Intake

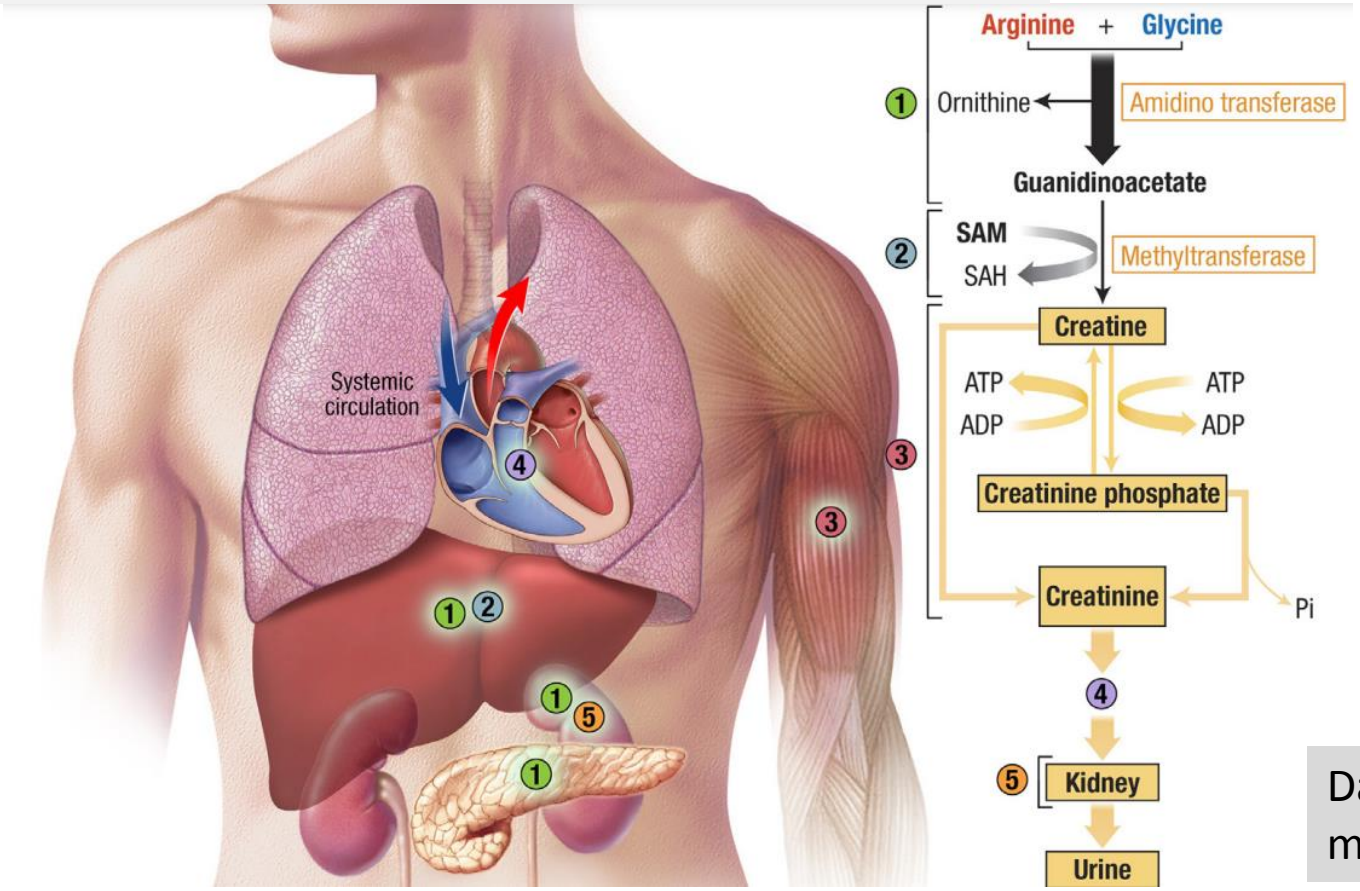
1. **Measuring urinary urea or nitrogen excretion** (objective methods, reflect the intake over only a few days before urine collection, not for protein source intake or other macronutrients)
2. **Self-reporting food intake via 24-h dietary recall**
3. **Food diary,** A 3- or 4-day food diary contains a complete record of foods and beverages consumed over those days
4. **Food frequency questionnaire (FFQ),** is widely used to investigate food intake over extended periods of time

- ✓**Creatine**
- ✓Protein
- ✓Anabolic androgenic steroids /GH
- ✓vitamins

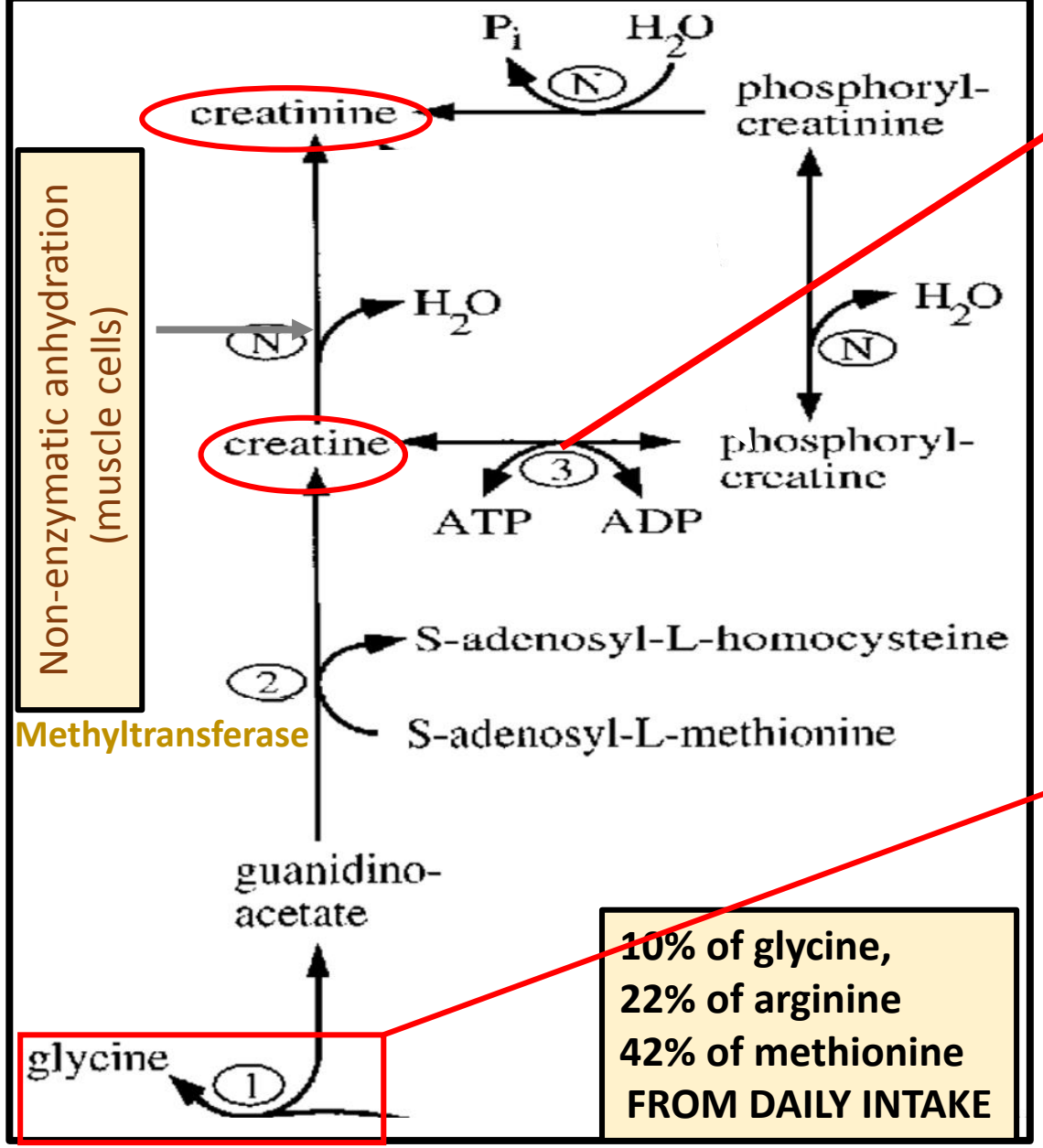
Creatine phosphate → available source of energy, especially during the early phases of intense muscular contractions.

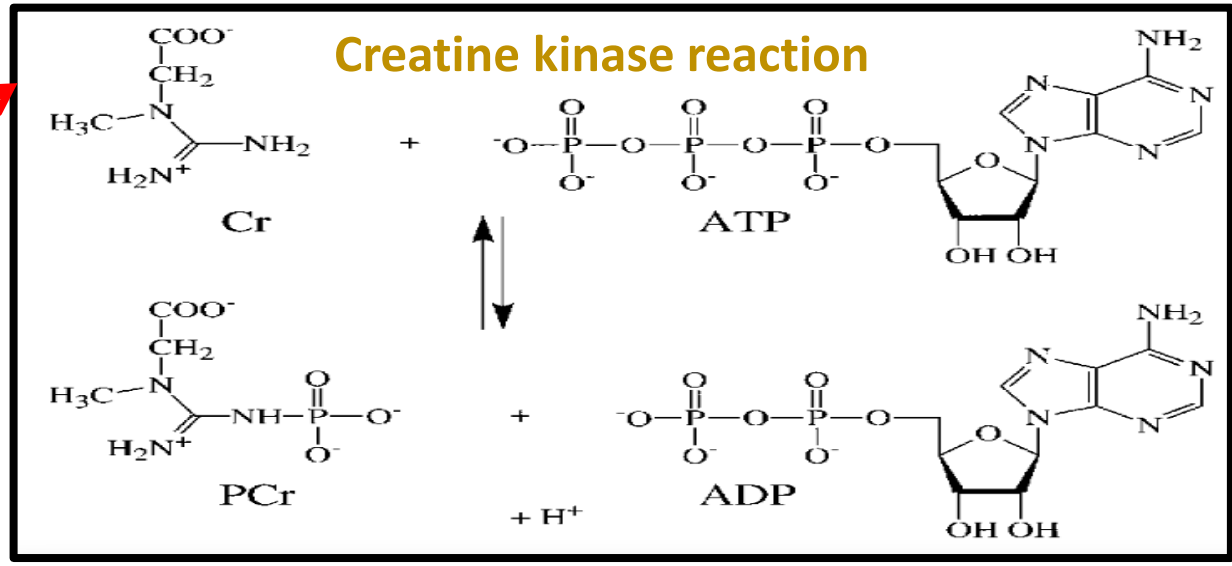
In skeletal muscle

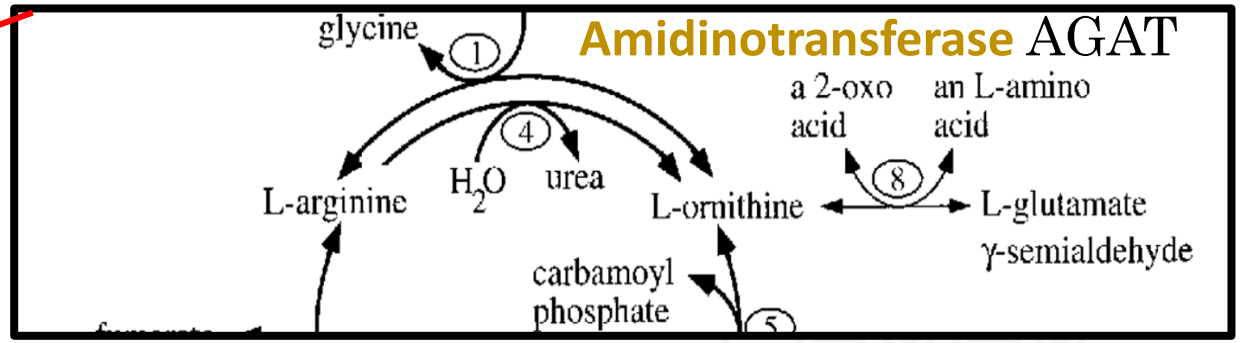
25% free creatine, 75% creatine phosphate **are in equilibrium**



Daily spontaneous degradation of **(1–2%)** muscle creatine→ **creatinine**


Pi
H2O
creatinine
phosphoryl-creatinine
Non-enzymatic anhydration (muscle cells)
H2O
H2O
creatine
phosphoryl-creatine
ATP
ADP
S-adenosyl-L-homocysteine
Methyltransferase
S-adenosyl-L-methionine
guanidino-acetate
glycine
10% of glycine,
22% of arginine
42% of methionine
FROM DAILY INTAKE


Creatine kinase reaction
Cr
ATP
PCr
ADP
+ H+


Amidinotransferase AGAT
glycine
a 2-oxo acid
an L-amino acid
L-arginine
H2O
urea
L-ornithine
L-glutamate γ-semialdehyde
carbamoyl phosphate

20 gram loading for 5 days ,then 5 gram daily

Creatine Supplements

Creatine Powder

Creatine HCL

Allmax Creatine

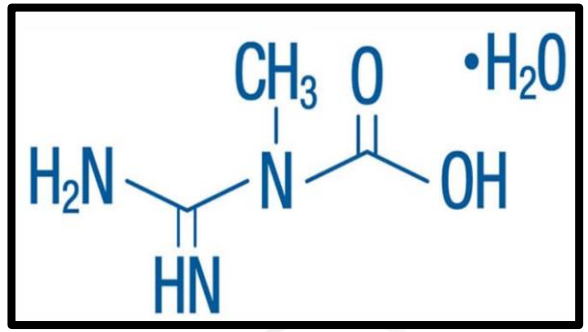
Creatine Tablets

Micronized Creatine

GNC Creatine

Creapure Creatine

Creatine Monohydrate



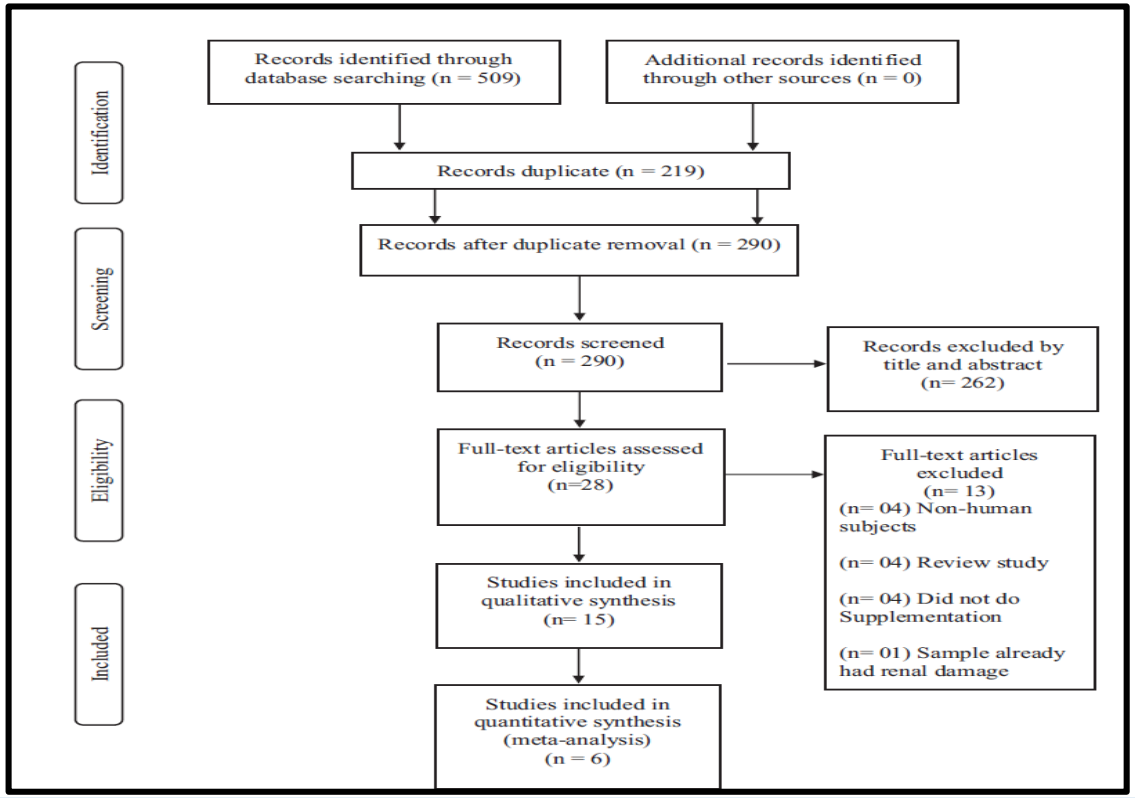
REVIEW ARTICLE

Effects of Creatine Supplementation on Renal Function: A Systematic Review and Meta-Analysis

Journal of Renal Nutrition
The Official Journal of the Council on Renal Nutrition of the National Kidney Foundation,
30 Jul 2019, 29(6):480-489

After evaluating 290 non-duplicated studies,

15 were included in the qualitative analysis
6 in the quantitative analysis



509 records in the 4 electronic databases (PubMed, Web of Science, SciELO, and Cochrane).

Eligible based on the following inclusion criteria

(1) randomized controlled trials
(2) published in peer-reviewed scientific journals
(3) case studies
(4) studies assessing creatine supplements and kidney effects

Journal of Renal Nutrition, 2019

Do not affect kidney function

No	Author(s)	Title	Age (y)	Supplementation Program (Protocol)			Conclusion Regarding Creatine Supplementation	Journal
				Type of Supplement	Daily and Weekly Quantities	Period in Days and Weeks		
1	Robinson et al.[37]	Dietary creatine supplementation does not affect some haematological indices, or indices of muscle damage and hepatic and renal function	26 ± 8	Creatine	5 g/d 4 times a day for 5 d, then 3 g/d for 8 wk	8 wk and 5 d	Do not affect kidney function	Br J Sports Med
2	Robinson et al.[37]	Dietary creatine supplementation does not affect some haematological indices, or indices of muscle damage and hepatic and renal function	27 ± 6	Creatine	5 g/d 4 times a day for 5 d, then 3 g/d for 8 wk	8 wk and 5 d	Do not affect kidney function	Br J Sports Med
3	Lugaresi et al.[34]	Does long-term creatine supplementation impair kidney function in resistance-trained individuals consuming a high-protein diet?	27 ± 5* 24 ± 3	Creatine monohydrate	20 g/d for 5 d, divided into 4 times daily, followed by 5 g/d throughout the trial	12 wk	Do not affect kidney function	J Int Soc Sports Nutr
4	Gualano et al.[15]	Creatine supplementation does not impair kidney function in type 2 diabetic patients: a randomized, double-blind, placebo-controlled, clinical trial	56.4 ± 8.2* 57.5 ± 5.0	Creatine monohydrate	5 g/d once daily	12 wk	Do not affect kidney function	Eur J Appl Physiol
5	Mayhew et al.[38]	Effects of long-term creatine supplementation on liver and kidney functions in American college football players	20.1 ± 0.8* 20.5 ± 1.4	Creatine monohydrate	Between 5 and 20 g/d (13.9 ± 5.8 g) for 5 y and 6 mo	~132 wk	Do not affect kidney function	Int J Sport Nutr Exerc Metab
6	Cancela et al.[40]	Creatine supplementation does not affect clinical health markers in football players	19.6 ± 3.5	Creatine monohydrate	4.4 g of creatine 3 times a day for 7 d, then 2.6 g creatine each day for 49 d	12 wk and 1 d	Do not affect kidney function	Br J Sports Med
7	Kreider et al.[16]	Long-term creatine supplementation does not significantly affect clinical markers of health in athletes	19.2 ± 2	Creatine monohydrate with carbohydrate drink	15.75 g/d for 5 d and an average of 5 g/d thereafter in 5-10 g doses following supervised training sessions	0-6 mo 7-12 mo 12-21 mo	Do not affect kidney function	Mol Cell Biochem
8	Carvalho et al.[4]	Creatine supplementation associated with resistance training does not alter renal and hepatic functions	23.0 ± 3.2* 24.3 ± 4.9	Creatine monohydrate	20 g/d divided into 4 times daily for 7 d and 0.03 g/kg body weight/day of creatine monohydrate for 7 wk	8 wk	DO not affect kidney function	Rev Bras Med Esporte
9	Carvalho et al.[4]	Creatine supplementation associated with resistance training does not alter renal and hepatic functions	23.0 ± 3.2* 25.2 ± 7.4	Creatine monohydrate	20 g/d divided into 4 times daily for 7 d and 5 g/d for 7 wk	8 wk	Do not affect kidney function	Rev Bras Med Esporte
10	Groeneveld et al.[5]	Few adverse effects of long-term creatine supplementation in a placebo-controlled trial	58.4 ± 10.9* 57.7 ± 11.1	Creatine monohydrate	5 g/d 2 times daily	4 wk 8 wk 16 wk 32 wk 48 wk At any time	Do not affect kidney function	Int J Sports Med
11	Gualano et al.[44]	Effects of creatine supplementation on renal function: a randomized, double-blind, placebo-controlled clinical trial	24.6 ± 4.2* 24.2 ± 5.0	Creatine	0.3 g/d/kg of body weight for the first week, and 0.15 g/d/kg of body weight for the next 11 wk	12 wk	Do not affect kidney function	Eur J Appl Physiol
12	Neves et al.[35]	Effect of creatine supplementation on measured glomerular filtration rate in postmenopausal women	57 ± 3* 59 ± 3	Creatine monohydrate	20 g/day for 7 d divided into 4 equal doses, followed by single doses of 5 g/d for the next 11 wk	12 wk	Do not affect kidney function	Appl Physiol Nutr Metab
13	Poortmans et al.[41]	Effect of short-term creatine supplementation on renal responses in men	25.1 ± 2.7	Creatine monohydrate	20 g/d divided into 4 times daily for 5 d	5 d	Do not affect kidney function	Eur J Appl Physiol

Journal of Renal Nutrit

Case reports of affecting kidney function

Table 2. Results of Studies of Creatine Supplementations' Effects (n = 4) on Renal Function in Case Studies

No	Author(s)	Title	Age (y)	Supplementation Program (Protocol)			Conclusion Regarding Creatine Supplementation	Journal
				Type of Supplement	Daily and Weekly Quantities	Period in Days and Weeks		
1	Taner et al.[42]	The effects of the recommended dose of creatine monohydrate on kidney function: case report	18	Creatine monohydrate	20 g/d for 5 d and maintenance (1 g/d for the next 6 wk)	5 d and 6 wk	Affects kidney function	Nephrol Dial Transplant
2	Thorsteinsdottir et al.[39]	Acute renal failure in a young weight lifter taking multiple food supplements, including creatine monohydrate: case study	24	Creatine	5 g/d 3 times per week, totaling 15 g/wk	24 wk	Affects kidney function	J Ren Nutr
3	Gualano et al.[36]	Effect of short-term high dose creatine supplementation on measured GFR in a young man with a single kidney: case report	20	Creatine monohydrate	20 g/d for 5 d divided into 4 equal doses, followed by single doses of 5 g/d for the next 30 ds	5 d and 4 wk	Do not affect kidney function	Am J Kidney Dis
4	Barisic et al.[43]	Effects of oral creatine supplementation in a patient with MELAS phenotype and associated nephropathy: case report	18	Creatine monohydrate	20 g/d, given in 4 single dosages for 12 d, and followed by a maintenance dosage of 5 g/d	12 d and 112 wk	Affects kidney function	Neuropediatrics

NDT Plus (2011) 4: 23–24
doi: 10.1093/ndtplus/sfq177
Advance Access publication 11 October 2010

Case Report

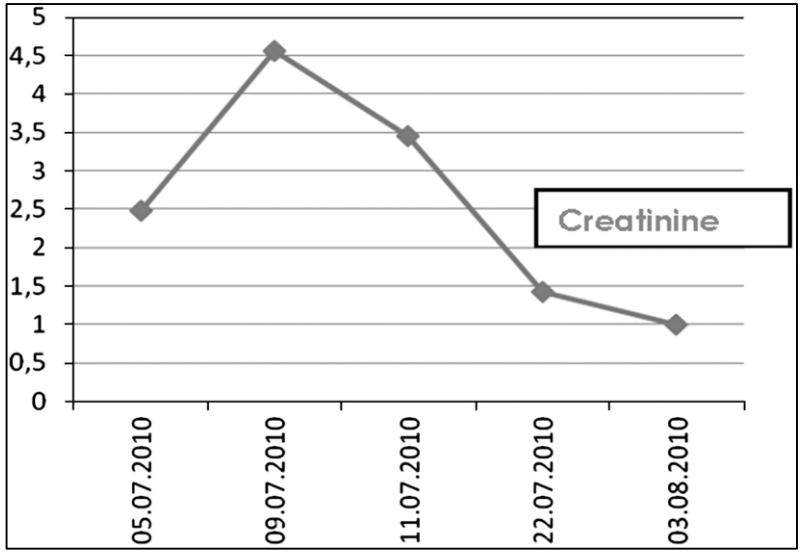
NDT PLUS
Nephrology Dialysis Transplantation

The effects of the recommended dose of creatine monohydrate on kidney function

Healthy 18y/o man, 2-day history of N,V and epigastric pain.
No signif PMHx/FHx,

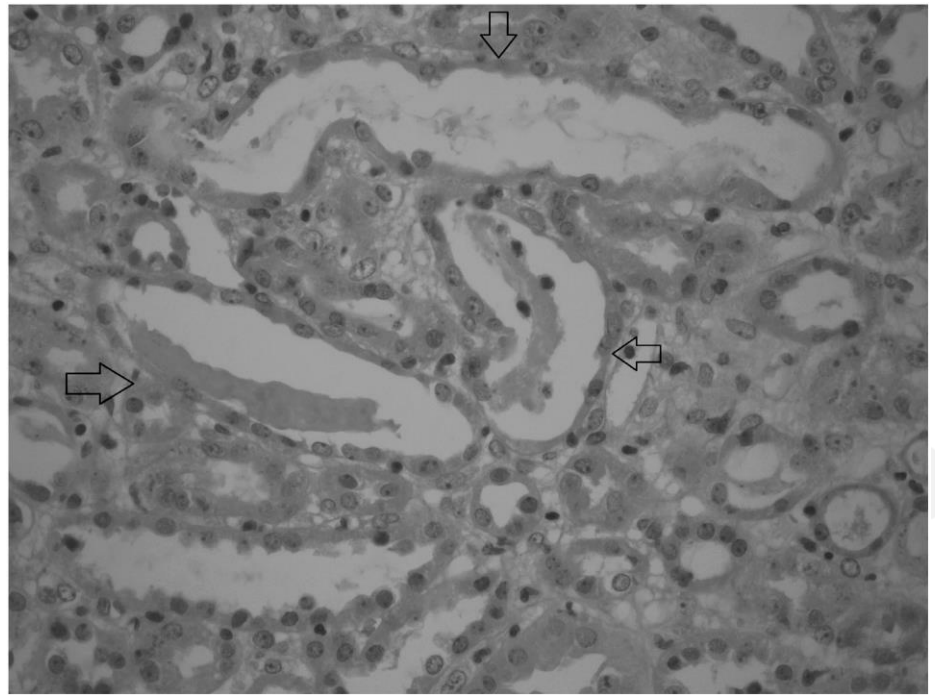
74/Kg, BMI=24.18 kg/m2, Bpx 150/90 mmHg, K=3.56 ,Na=148 mmol/L, Ph= 7.36, Hct 36.8, T.protein 64.87 g/L (normal 64–87 g/L). UA→ proteinuria, daily 284 mg. The other Lab test and 2nd W/U were normal.

Creatine monohydrate, induction (20 g/day ×5 /d) and maintenance (1 g/day for the next 6 weeks).



He was discharged without any complaints on the 25th day, BW=72Kg.

- Focal tubular injury with dilatation of tubular lumina and flattening of the tubular epithelial cells,
- sloughed epithelial cells, leucocytes and cellular debris in the tubular lumina;
- No pigmented casts
- Normal glomeruli.
- IF→ Neg



CASE STUDY

Acute Renal Failure in a Young Weight Lifter Taking Multiple Food Supplements, Including Creatine Monohydrate

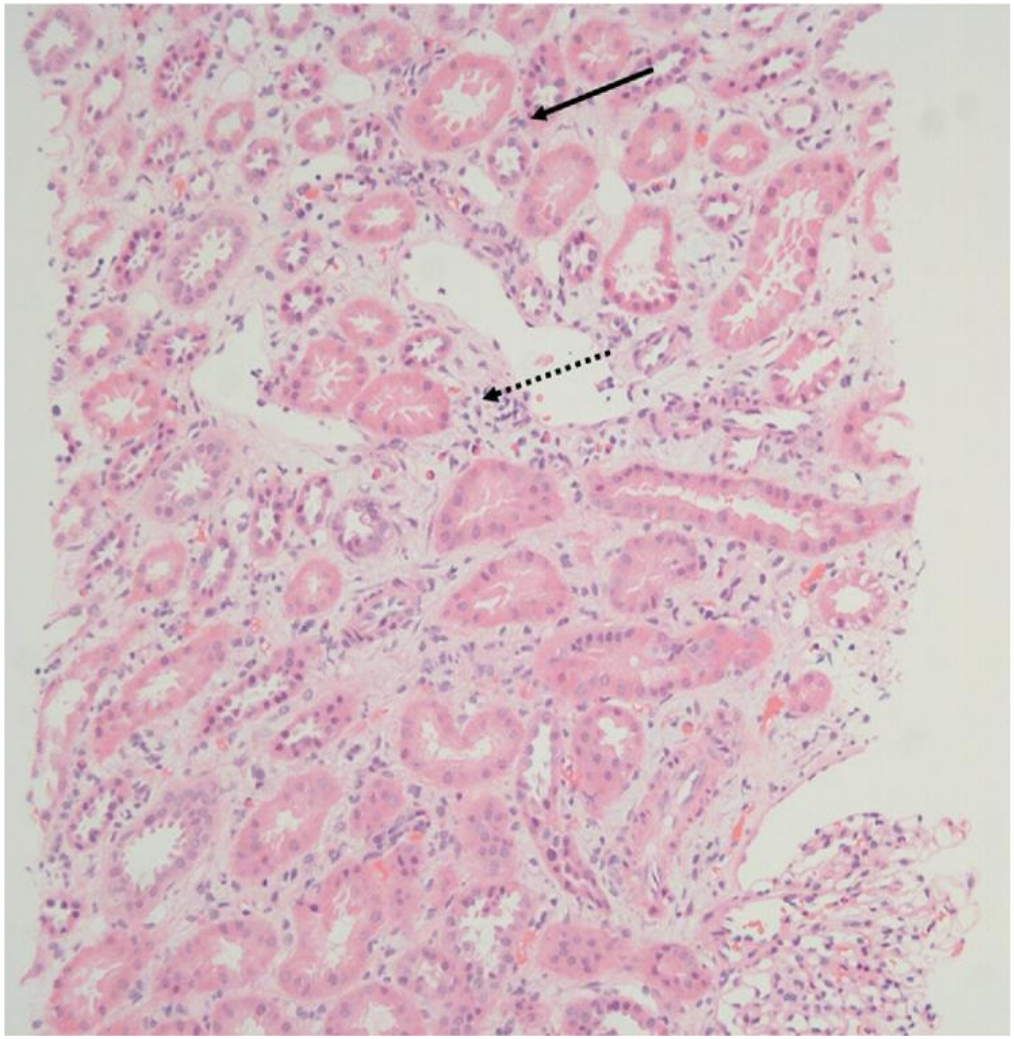
Journal of Renal Nutrition, 2019

A previously healthy 24-y/o man, acute abdominal pain, polydipsia, and polyuria. BPx=152/100 mm Hg,left flank tenderness. Cr=3.8 mg/dL, initially increased to 4.7 mg/dL and then rapidly decreased to 2.5 mg/dL, proteinuria 386 mg/day, UA→1 to 3 RBCs, The other Lab test and 2nd W/U were normal.
5 days after the onset of symptoms, no proteinuria, normal GFR, and normotensive in OPD f/u.

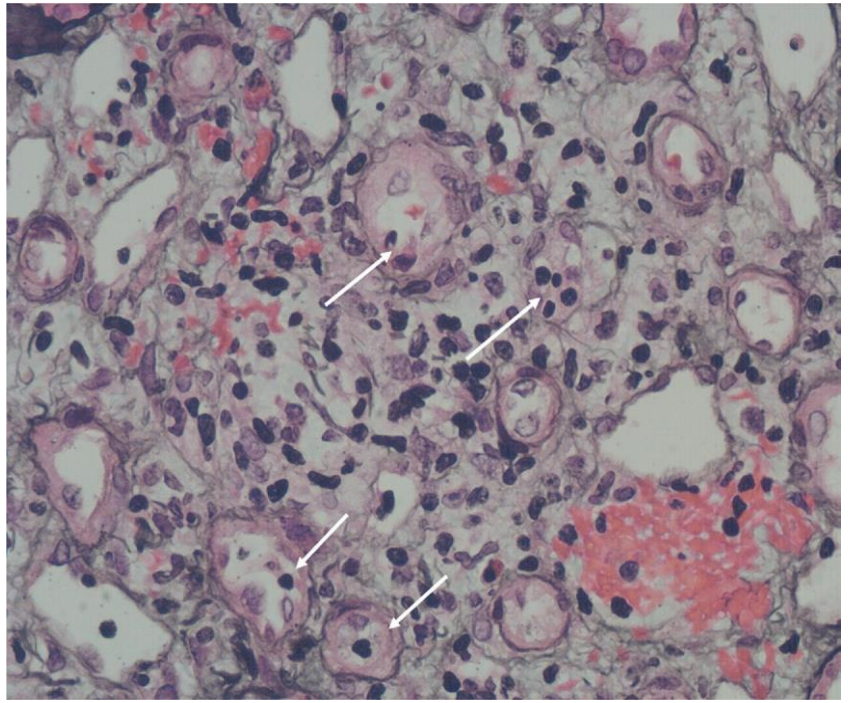
Table 1. List of Dietary Supplements That the Patient Was Taking at the Time of Admission*

Amino Acids	Plant Extracts	Other Supplements
L-alanine 620 mg	Dandelion leaf	Creatine monophosphate 5 g (15 g/week)
L-arginine 285 mg	Uva ursi	Choline bitartrate
L-aspartic acid 1,200 mg	Grean tea	Inositol
L-cystine 380 mg	Peppermint	Phosphatidylcholine 75 mg
L-glutamic acid 1990 mg	Ginger	Phosphorus 2,120 mg
Glycine 225 mg	Licorice	Folic acid 400 μg
L-histidine 180 mg	Chamomile	Niacin 40 mg
L-isoleucine 825 mg	Hawthorn	Calcium 53 mg
L-leucine 1,220 mg	Cassia	Iron 2.2 mg
L-lysine 1,050 mg	Mate	Chondroitin sulfate
L-methionine 240 mg	Chicory	Glucosamine HCl
Phenylalanine 360 mg	Citrus fruit	Sodium 375 mg
L-proline 790 mg	Guarana seed	Potassium 200 mg
L-serine 575 mg	Cotinue coggygyria	Choline bitartrate
L-tryptophan 165 mg	Scop bark	Inositol
L-tyrosine 345 mg	Red panax ginseng	Phosphatidylcholine 75 mg
L-valine 720 mg	Garcinia cambogia	Acetyl L-carnitine
	Caffeine	

*Values represent daily oral intake; left blank when not quantified.



Interstitium interstitial edema and a lymphocytic inflammatory infiltrate with <u>focal interstitial hemorrhage</u>, Arrows point to areas of tubulitis.



generalized interstitial edema, infiltrate,most prominent in the juxtamedullary cortex and medulla, lymphocytes admixed with eosinophils

IF→ were negative.

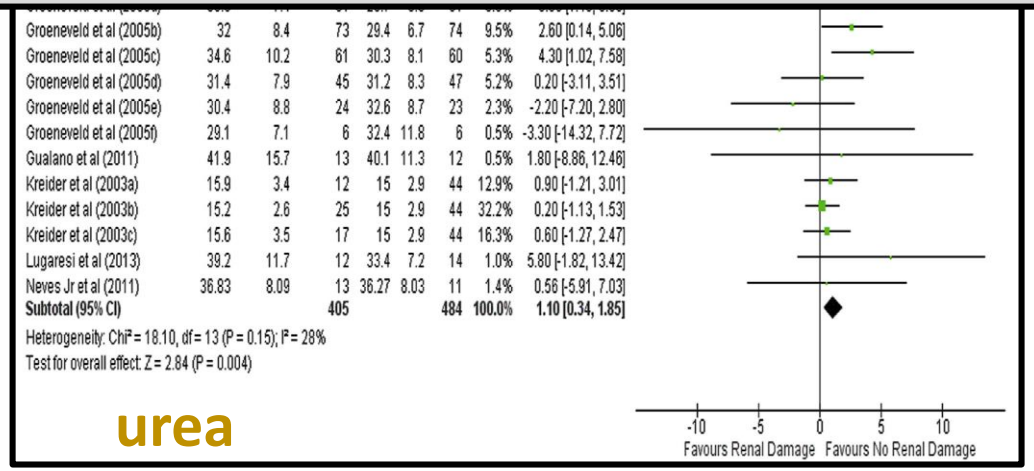
EM→
normal glomerular architecture, without evidence of immune complex deposition.

REVIEW ARTICLE

Effects of Creatine Supplementation on Renal Function: A Systematic Review and Meta-Analysis

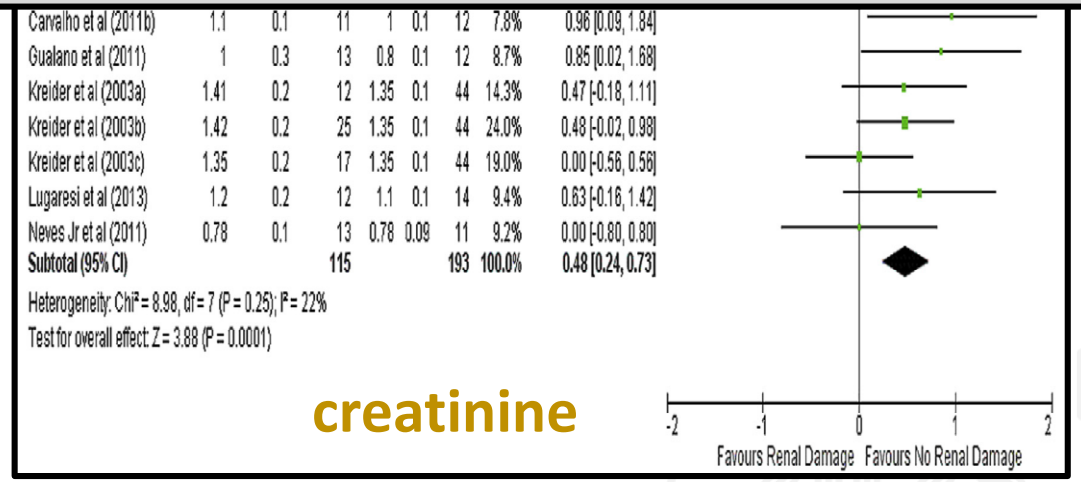
Effects of creatine supplementation on urea and creatinine

The findings indicate that creatine supplementation does not induce renal damage in the studied amounts and durations



urea

(standardized mean difference = 1.10, 95% confidence interval 0.34-1.85, P = .004, I^2 = 28%).



creatinine

(standardized mean difference = 0.48, 95% confidence interval 0.24-0.73, P = .001, I^2 = 22%),

- ✓Creatine
- ✓**Protein**
- ✓Anabolic androgenic steroids /GH
- ✓vitamins

Protein Supplementation

Plants proteins: pulses, such as nuts, dried peas, and lentils, (have HP content)

Milk protein (whey or casein), good quality protein

Eggs

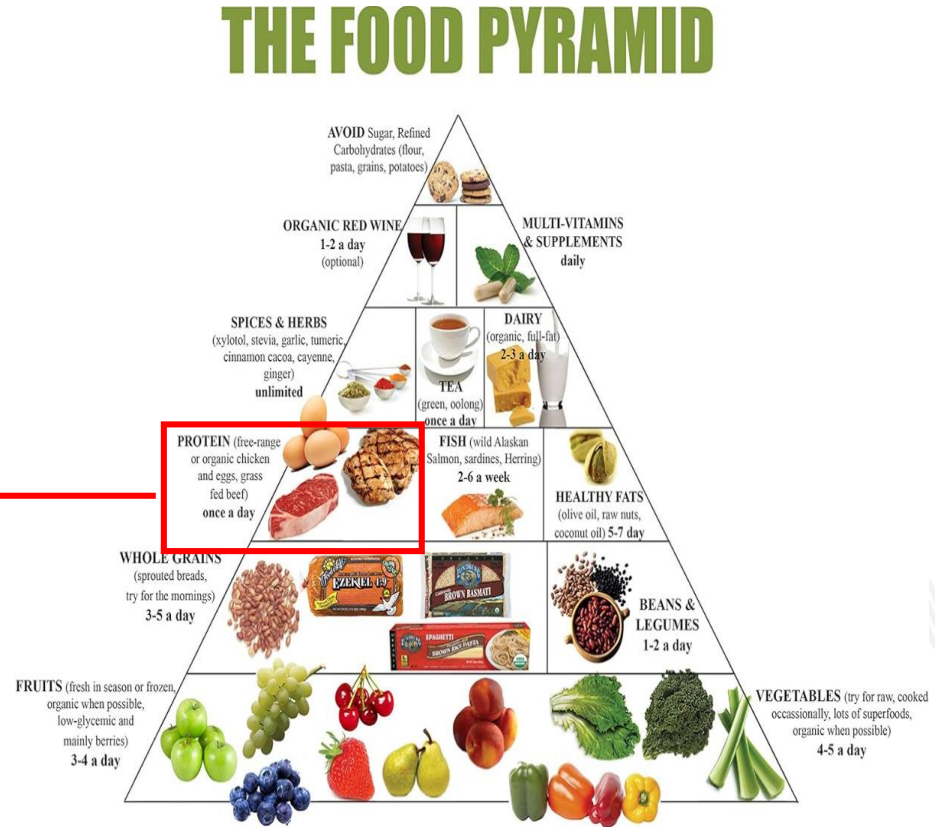
Red meat: Beef, pork, mutton, and game (e.g., reindeer and moose)

White meat: chicken and turkey

Meat, fish, cheese, and rice / other grains→**strong net-acidifying foods**

Fruit, legumes, vegetables, and potatoes →**strong net-alkalinizing foods**

u-eat/vegetables-and-fruits/



ACUTE EFFECT OF HIGH-PROTEIN ON GFR

SINGLE MEAL	6 healthy individuals	Non-albuminuric T2DM
Tuna fish	Rise in measured GFR	Rise in measured GFR
Boiled egg (double the amount of Tuna fish protein)	Did not change GFR	Did not change GFR
Beef (200 g)	Rise in measured GFR	
Vegetable protein Equal amount to beef (baked skim soy with soy sauce, which has an amino acid composition similar to beef)	Rise in measured GFR	

Conflicting effects of HP intake on GFR and urinary albumin excretion in human studies

PROTEIN INTAKE

	good quality protein g/kg/day	energy consumption (E%)
WHO recommendations **General population**	**0.83**	**10–35%**
Nordic Nutrition Recommendations **Elderly** **<64 y/o** **>= 65 y/o**	**0.8–1.5** **1.1–1.3**	**10–20 %** **15–20 %**
Athletes	**1.2–1.7**	
Chronic Kidney Disease	**0.8**	
Diabetes	**1–1.5**	**15– 20%**

High-Protein Diets

Protein content of more than **25 E% of energy intake**, which corresponds to more than **2.0 g protein/kg BW daily**.

Research Article

Journal of Nutrition and Metabolism, 2016
.doi.org/10.1155/2016/9104792

A High Protein Diet Has No Harmful Effects: A One-Year Crossover Study in Resistance-Trained Males

Jose Antonio, Anya Ellerbroek, Tobin Silver, Leonel Vargas, Armando Tamayo, Richard Buehn, and Corey A. Peacock

14 healthy resistance-trained men completed the randomized crossover study

(mean age 26.3 ± 3.9 yr, height 178.5 ± 8.4 cm; and average years of training 8.9 ± 3.4 yr).

10 white males, 3 black males, and 1 Pacific Islander

Food diary (i.e., three days per week for one year) of their food intake via a smartphone app (MyFitnessPal) ; 100–168 daily dietary self-reports

Body composition, via the Bod Pod (COSMED USA, Concord, CA) whole body densitometry using air displacement.

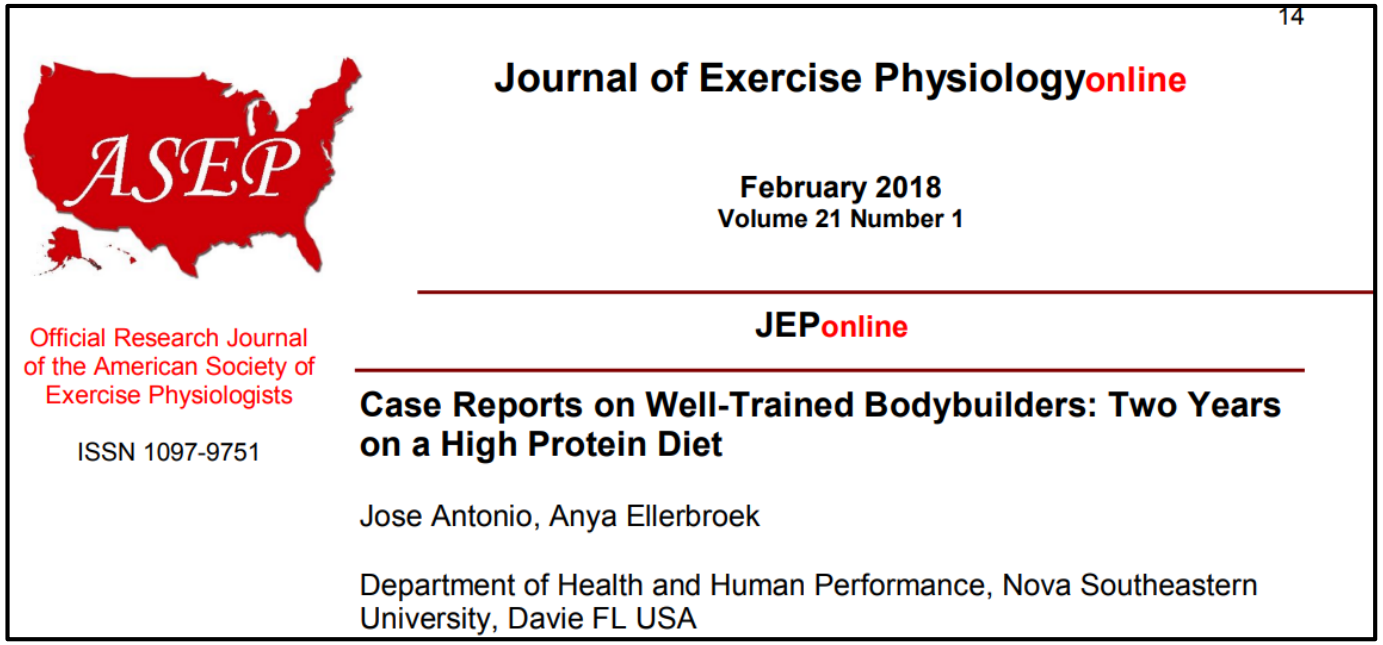
Glucose,BUN, CRE, GFR, Na, K , Cl, carbon dioxide, Ca, T protein, albumin, globulin, T Bili , ALP AST ALT, TG Chol, LDL HDL.

1. **Normal eating phase,** (mean ± SD) 29.94 ± 5.65 kcals/kg/day and 2.51 ± 0.69 g/kg/day of protein for 2 months and 4 months
2. **High protein phase,** to 34.37 ± 5.88 kcals/kg/day and 3.32 ± 0.87 g/kg/day of protein for 2 months and 4 months

(significantly increased ($p < 0.05$))

In resistance-trained men that consumed a high protein diet (~2.51–3.32 g/kg/d) for one year, there were no harmful effects on measures of blood lipids as well as liver and kidney function tests.

No deleterious effects on liver or kidney function



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Journal of Exercise Physiology online

February 2018
Volume 21 Number 1

Official Research Journal of the American Society of Exercise Physiologists

ISSN 1097-9751

JEP online

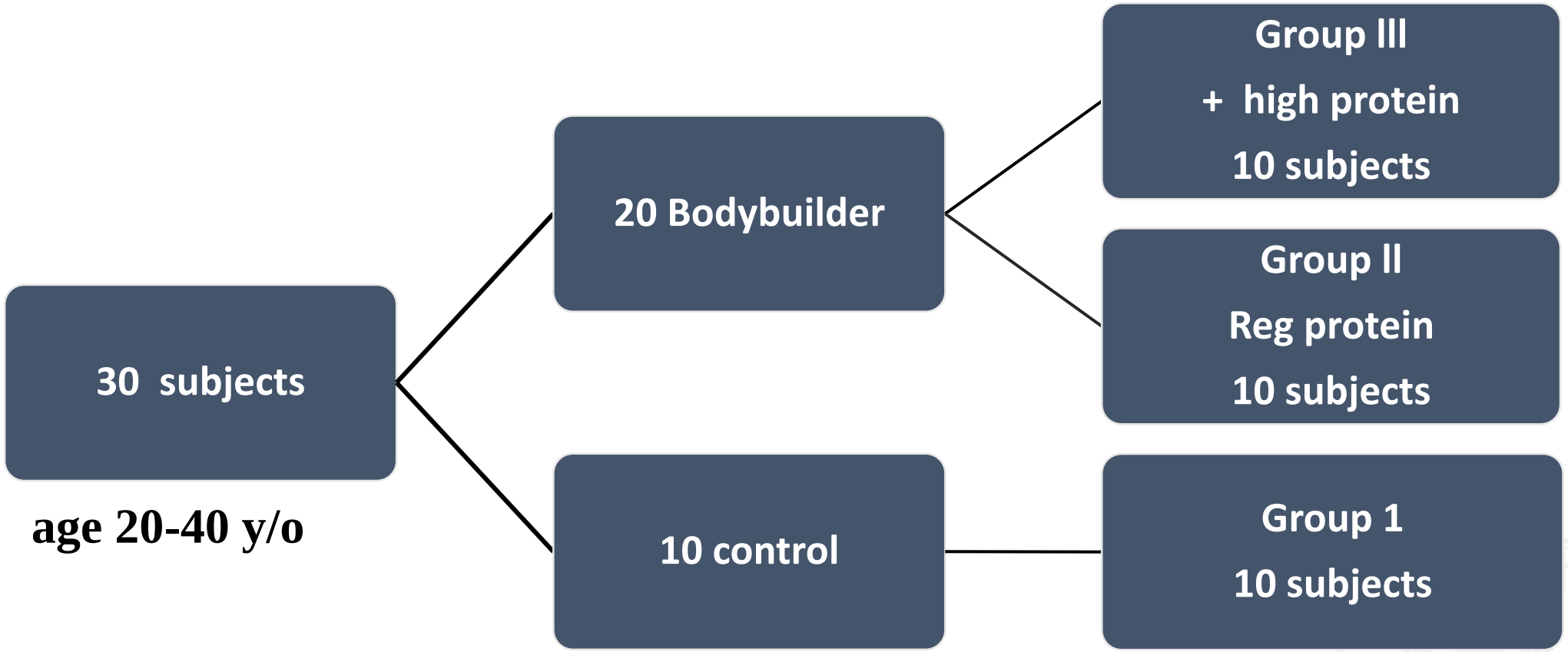
Case Reports on Well-Trained Bodybuilders: Two Years on a High Protein Diet

Jose Antonio, Anya Ellerbroek

Department of Health and Human Performance, Nova Southeastern University, Davie FL USA

Assess 5 subjects who consumed a high protein diet for a total of 2 yrs

Effects of a high protein intake on kidney function and acid excretion in bodybuilders



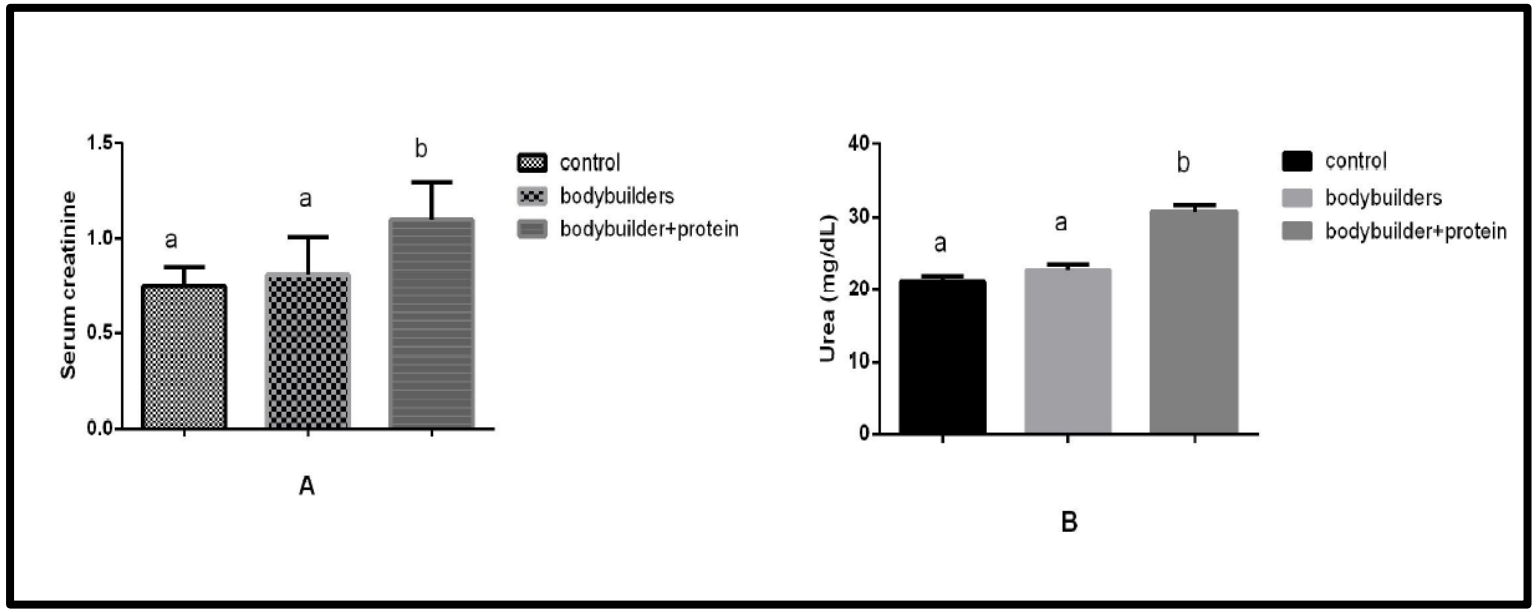
Resting blood samples taken between 8 and 9 am.

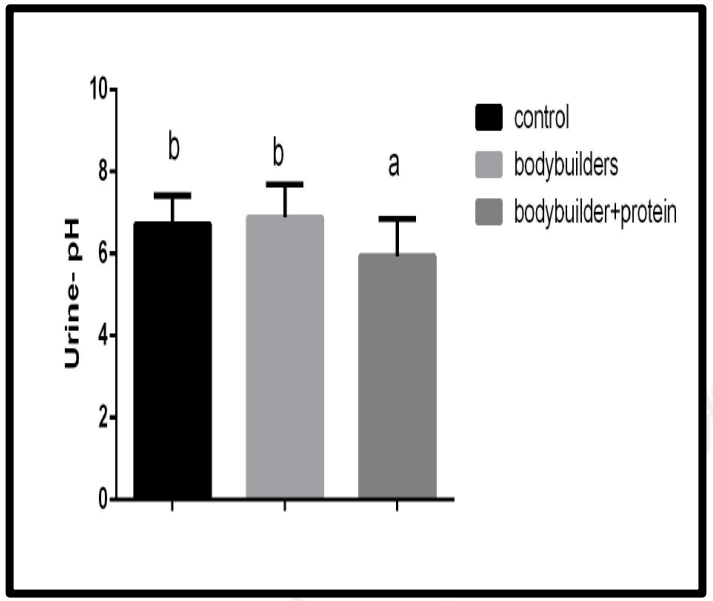
After an overnight fast 24- hour urine were obtained on 30 day of the study to measure pH and estimate kidney function

March 2020 DOI: 10.37200/IJPR/V24I7/PR270044

High protein intake in bodybuilders

1. Produced a significant increase in serum urea and creatinine.
2. Increase endogenous acid production,





Acute kidney injury associated with androgenic steroids and nutritional supplements in bodybuilders†

Four bodybuilders

Clin Kidney J. 2015 Aug

Safa E. Almukhtar,[1,2] Alaa A. Abbas,[3] Dana N. Muhealdeen,[3] and Michael D. Hughson[3]

Compler risk for permane

Wael El-Reshaid
John Patrick Madda

22 adult males,8 FSGS, 4 nephroangiosclerosis, 2 acute/ 3 chronic interstitial nephritis, 2 nephrocalcinosis, and 1 membranous with crescentic glomerulopathy,

Saudi J Kidney Dis Transpl .2018

REVIEW www.jasn.org

The Effects of High-Protein Diets on Kidney Health and Longevity

Gang-Jee Ko,[1,2] Connie M. Rhee,[1] Kamyar Kalantar-Zadeh,[1,3,4] and Shivam Joshi[5]

JASN, 2020. doi: https://doi.org/10.1681/ASN.2020010028

Summary of observational studies of high dietary protein intake and kidney health across large populations

1. **The Nurses' Health Study.**
2. **The Multiethnic Study of Atherosclerosis.**
3. **The Prevention of Renal and Vascular End-Stage Disease (PREVEND) study.**
4. **The Gubbio Study.**
5. **The Dutch Generation R Study.**
6. **The Framingham Heart Study.**
7. **The Cardiovascular Health Study.**
8. **The Singapore Chinese Health Study.**

Study Reference	Study or Location	Type	N (BMI, kg/m^2)	Mean Age (yr)	Mean eGFR (ml/min per 1.73 m^2)	DM/HTN HTx (%)	Sex (% male)	Protein Intake in the Highest Group (g/kg per d, g/d, or % of total calorie intake)	Duration (yr)	Variable and Outcome
Knight *et al.*[12]	Nurses' Health Study	Prospective cohort	1624 (N/D)	55	90	4/40	0	93 g/d	11	HP was not associated with eGFR decline in normal renal function. However, it was associated with accelerated eGFR decline in mild CKD
Huang *et al.*[74]	Taiwan	Cross-sectional	599 (24.3)	60	22	N/D	54	N/D	N/A	HP was also associated with worsening eGFR at increments of −3.50 ml/min per 1.73 m^2, compared with moderate and low protein intake ($P<0.001$)

nondairy protein was associated with rapid decline of eGFR among participants with mild CKD
animal fat/ red meat was associated with higher odds of microalbuminuria

Study Reference	Study or Location	Type	*N* (BMI, kg/m^2)	Mean Age (yr)	Mean eGFR (ml/min per 1.73 m^2)	DM/HTN HTx (%)	Sex (% male)	Protein Intake in the Highest Group (g/kg per d, g/d, or % of total calorie intake)	Duration (yr)	Variable and Outcome
Halbesma *et al.*[75]	Prevention of Renal and Vascular ENd-stage Disease (PREVEND)	Prospective cohort	8461 (26.1)	50	81	N/D	N/D	1.4 g/kg per d	7.0	No association between baseline protein intake and rate of renal function decline
Cirillo *et al.* [10]	Gubbio Study	Prospective cohort	1522 (28)	54	84	5/41	44	2.1 g/kg per d	12	1 g/d higher protein intake was related to −4.1 ml/min per 1.73 m^2 more negative eGFR change and 1.78 risk for incidence of eGFR <60 ml/min per 1.73 m^2
Beasley *et al.*[76]	Cardiovascular Health Study	Prospective cohort	3623 (26.5)	72	73	14/55	39	1.63 g/kg per d;24% of total calories	6.4	Protein intake was not associated with change in eGFR (P>0.05 for all comparisons)

Study Reference	Study or Location	Type	*N* (BMI, kg/m^2)	Mean Age (yr)	Mean eGFR (ml/min per 1.73 m^2)	DM/HTN HTx (%)	Sex (% male)	Protein Intake in the Highest Group (g/kg per d, g/d, or % of total calorie intake)	Duration (yr)	Variable and Outcome
Malhotra *et al.*[77]	Jackson Heart Study	Observational cohort	3165 (31.8)	55	97	19/57	36	1.0 g/kg per d;19.4%	8	Consumption of protein as percentage of energy intake in lowest and highest quintiles was associated with decline in eGFR among subjects who were diabetic
Esmeijer *et al.*[78]	Alpha Omega Cohort	Prospective cohort	2255 (27.6)	69	82	18/57	80	92 g/d17%	3.5	Patients with a daily total protein intake of ≥1.20 compared with <0.80 g/kg ideal body weight had a twofold faster annual eGFR cysC decline (−1.60 versus −0.84 ml/min per 1.73 m^2) in patients post-MI

Study Reference	Study or Location	Type	*N* (BMI, kg/m^2)	Mean Age (yr)	Mean eGFR (ml/min per 1.73 m^2)	DM/HTN HTx (%)	Sex (% male)	Protein Intake in the Highest Group (g/kg per d, g/d, or % of total calorie intake)	Duration (yr)	Variable and Outcome
Jhee *et al.*[79]	Korean Genome and Epidemiology Study	Prospective cohort	9226 (24.5)	52	94	7/14	48	1.7 g/kg per d	11.5	The highest quartile was associated with 1.32-fold increased risk of rapid eGFR decline (95% CI, 1.02 to 1.73)
Farhadnejad *et al.*[13]	Tehran Lipid and Glucose Study	Prospective cohort	1797 (26.7)	38	76	12/18	46	16%	6.1	The highest tertile of LCHP diet had greater risk of incident CKD (OR, 1.48; 95% CI, 1.03 to 2.15) in comparison to those in the lowest one (*P* for trend=0.027)

Study Reference	Study or Location	Type	*N* (BMI, kg/m^2)	Mean Age (yr)	Mean eGFR (ml/min per 1.73 m^2)	DM/HTN HTx (%)	Sex (% male)	Protein Intake in the Highest Group (g/kg per d, g/d, or % of total calorie intake)	Duration (yr)	Variable and Outcome
Lew *et al.*[51]	Singapore Chinese Health Study	Prospective cohort	63,257 (23)	57	N/D	9/23	43	65.3 g/d	15.5	Total protein intake was positively associated with incidence of ESKD in a model that adjusted for basic demographic characteristics

Highest quartile of protein intake (from red meat) had 40% increased HR of ESKD (dose dependent). Replacing one serving of red meat with other protein sources was associated with a max relative risk reduction of 62.4%

(i.e., age,gender, dialect, educational level, and year of interview: HR,1.55; 95% CI, 1.28 to 1.87) when comparing the highest quartile with the lowest quartile intake. However, the HR was attenuated to 1.19 (95% CI, 0.98 to 1.44)after adjusting for other lifestyle and comorbidity factors

CONCLUSION

- ✓These studies suggest that long-term intake of dietary protein above nutritional recommendations can increase the risk of serious CKD, including ESRD.

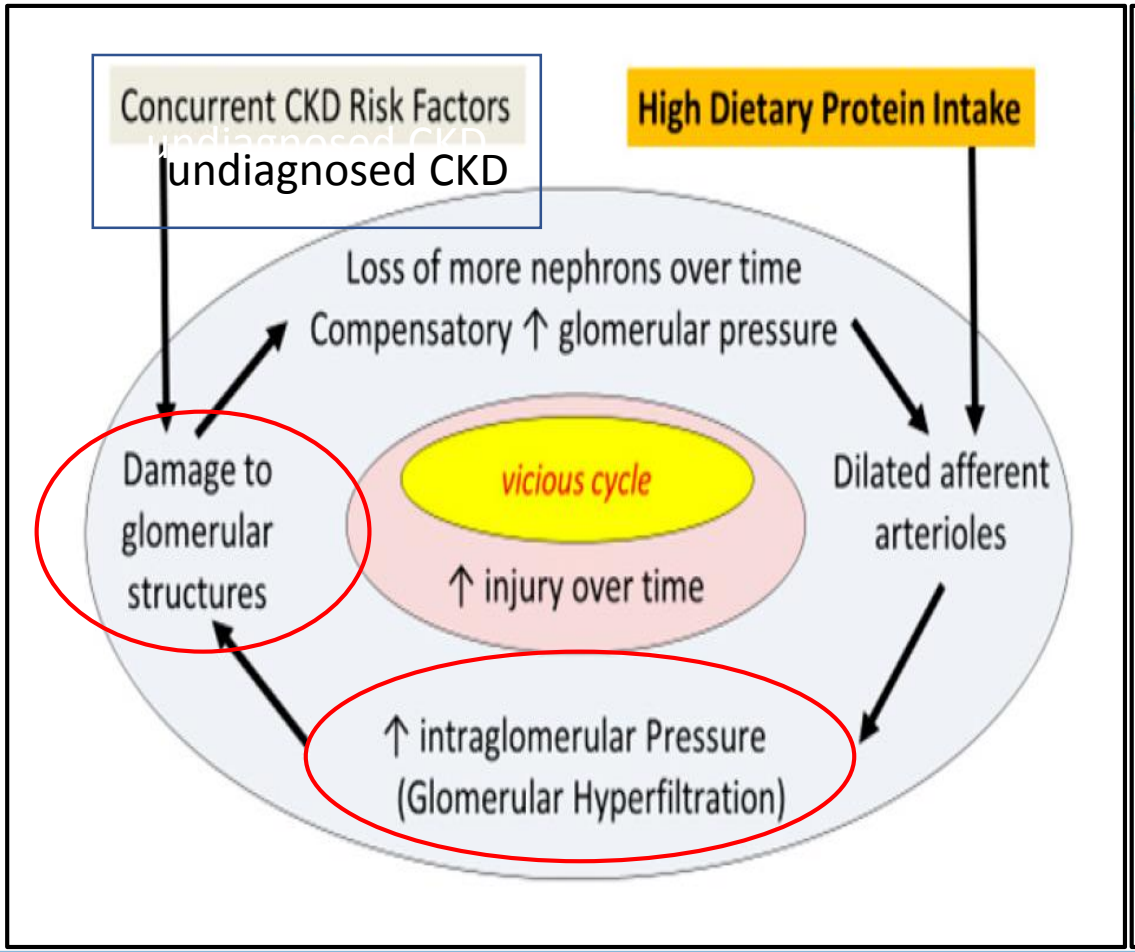
- ✓High intake of red meat protein and acidifying protein seems to be most harmful.

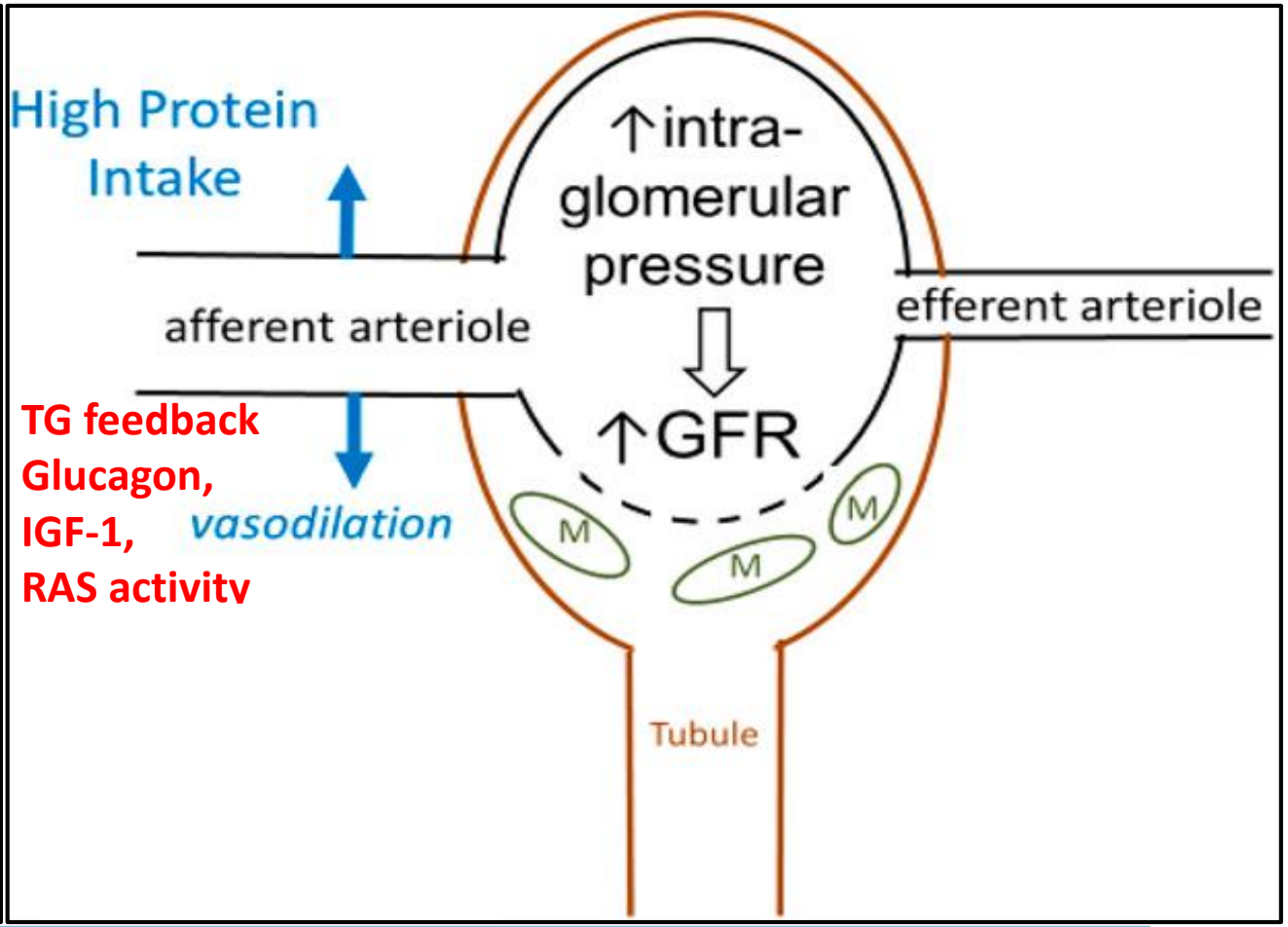
Oral protein or Amino Acid infusion →increase RBF and GFR (hyperfiltration)

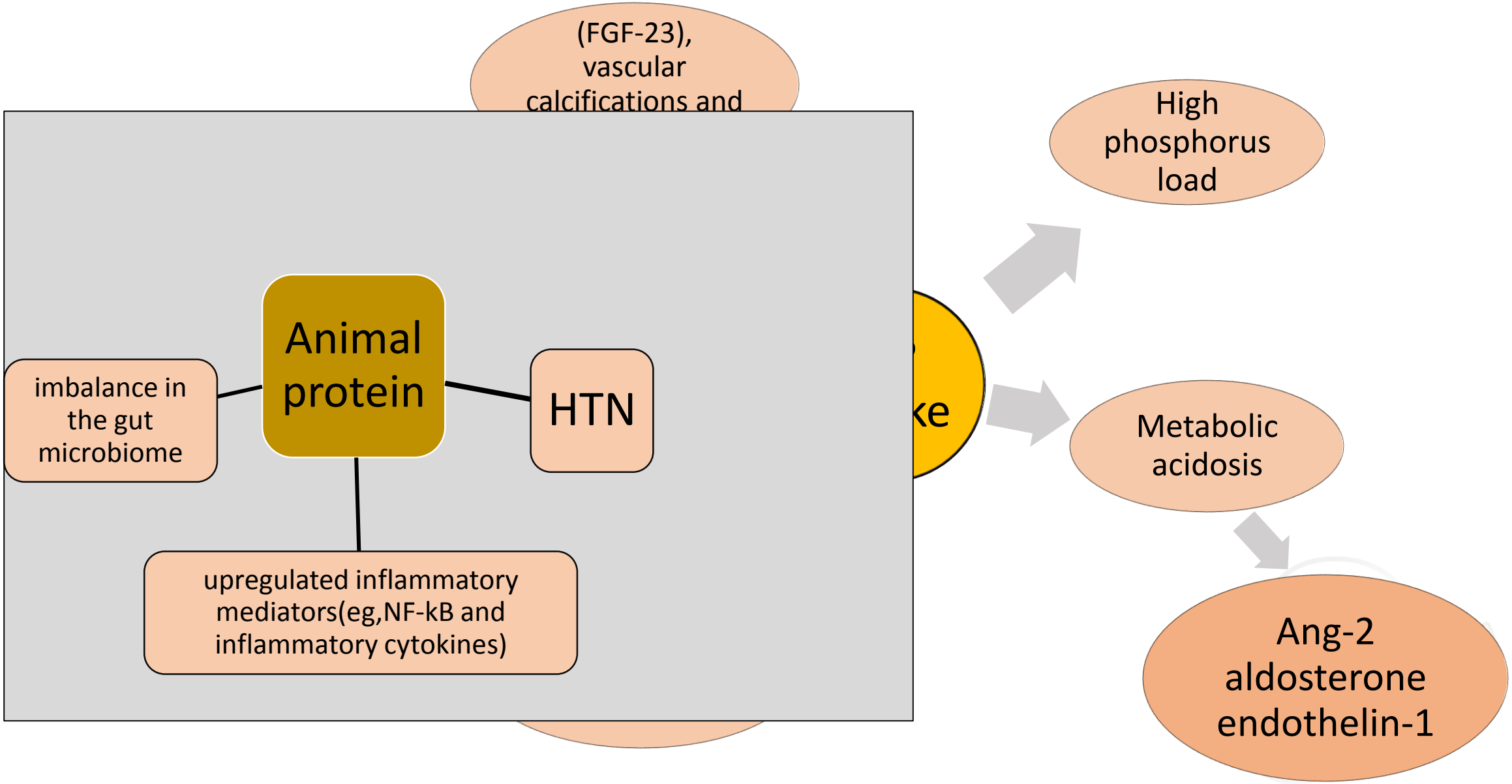
mesangial matrix expansion

Tubulointerstitial fibrosis

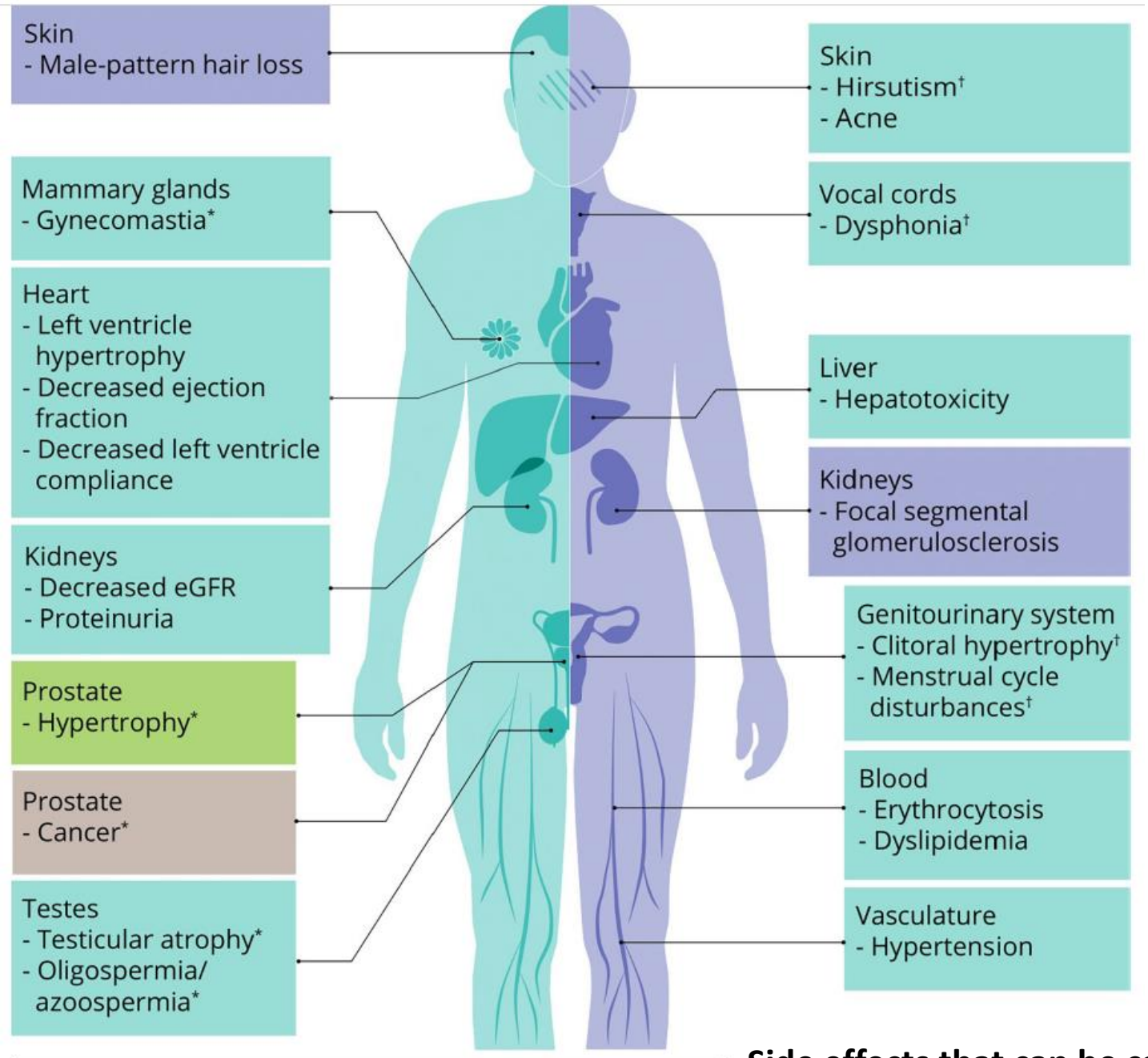
Kidney enlargement






(FGF-23),
vascular
calcifications and
Animal
protein
imbalance in
the gut
microbiome
HTN
upregulated inflammatory
mediators(eg,NF-kB and
inflammatory cytokines)
ke
High
phosphorus
load
Metabolic
acidosis
Ang-2
aldosterone
endothelin-1

- ✓Creatine
- ✓Protein
- ✓**Anabolic androgenic steroids / GH**
- ✓vitamins



Side effects that can be caused by AAS

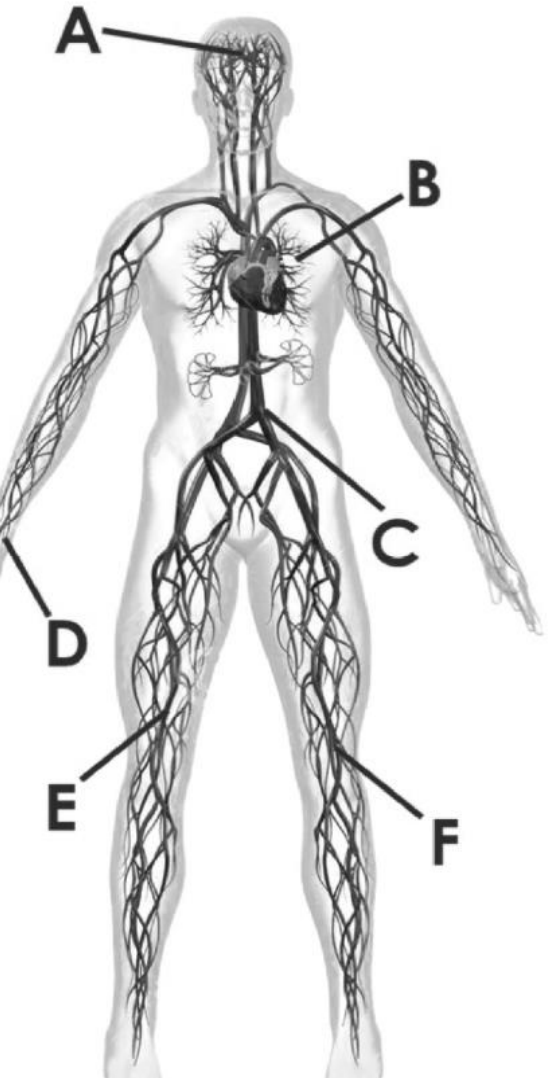
In 2014 the global lifetime use prevalence was **3.3%**,

Athletic use;13.4% while
Recreational sports people; **18.4%**

In the Middle east **(21.7%)**
South America, (4.8%)
Europe (3.8%)

Frontiers in Endocrinology 2022

Cardiovascular adverse effects due to a prolonged use of AAS



Cardiovascular effects

A. Cerebrovascular ischaemic events
Superior saggital sinus thrombosis

B. Pulmonary embolism
Coronary disease
Reduced systolic function
Distolic dysfunction - relaxation abnormally
Arrhytmias
Myocardial infarction
Sudden death arrhytmias - sudden death
Left ventricular hypertrophy

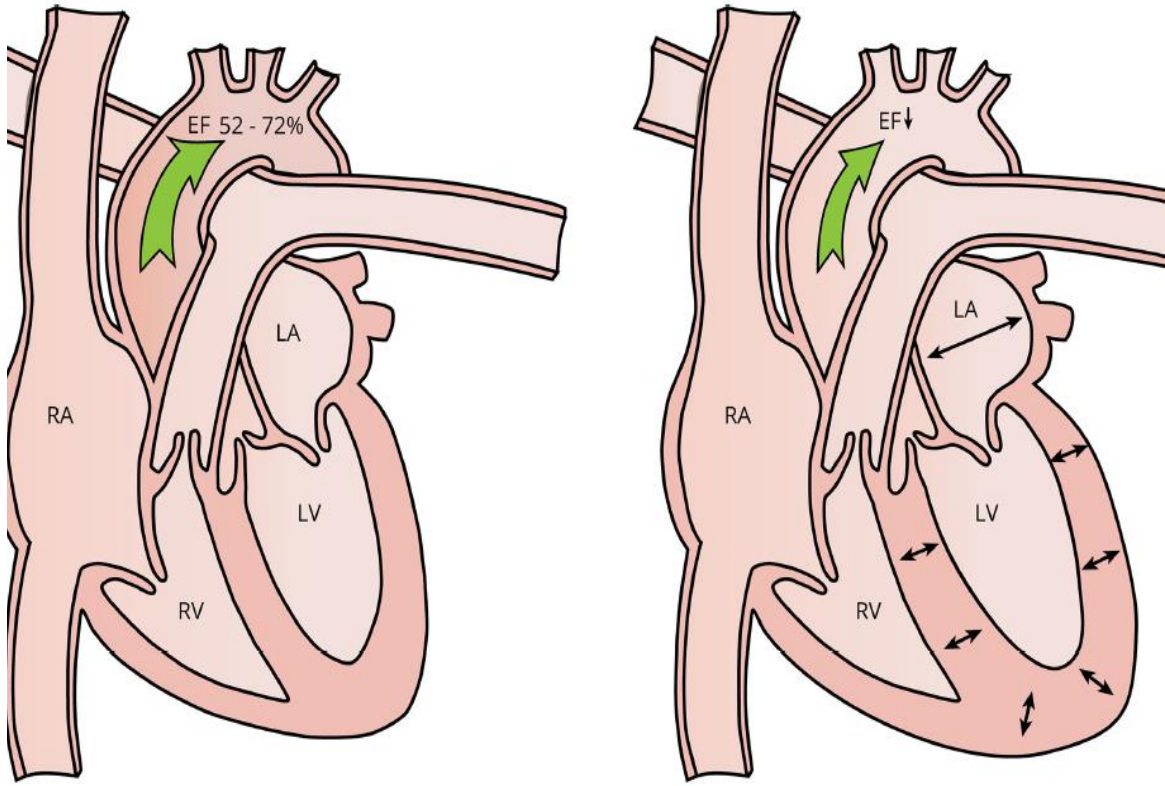
C. Blood pressure elevation
Pro-atherogenic effects

D. Alterated vascular reactivity

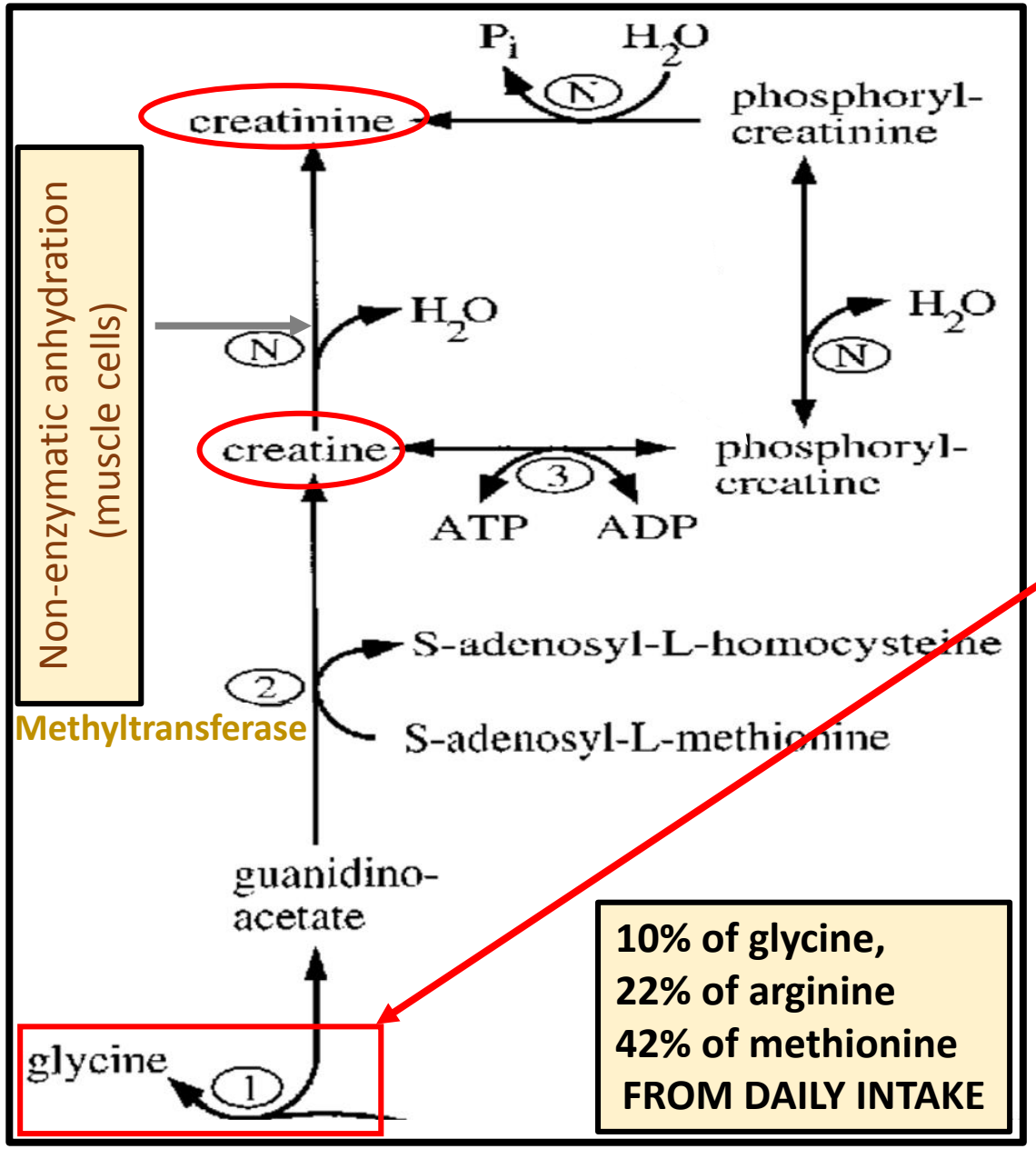
E. Peripheral arterial disease

F. Deep venous thrombosis

remodeling induced by AAS use

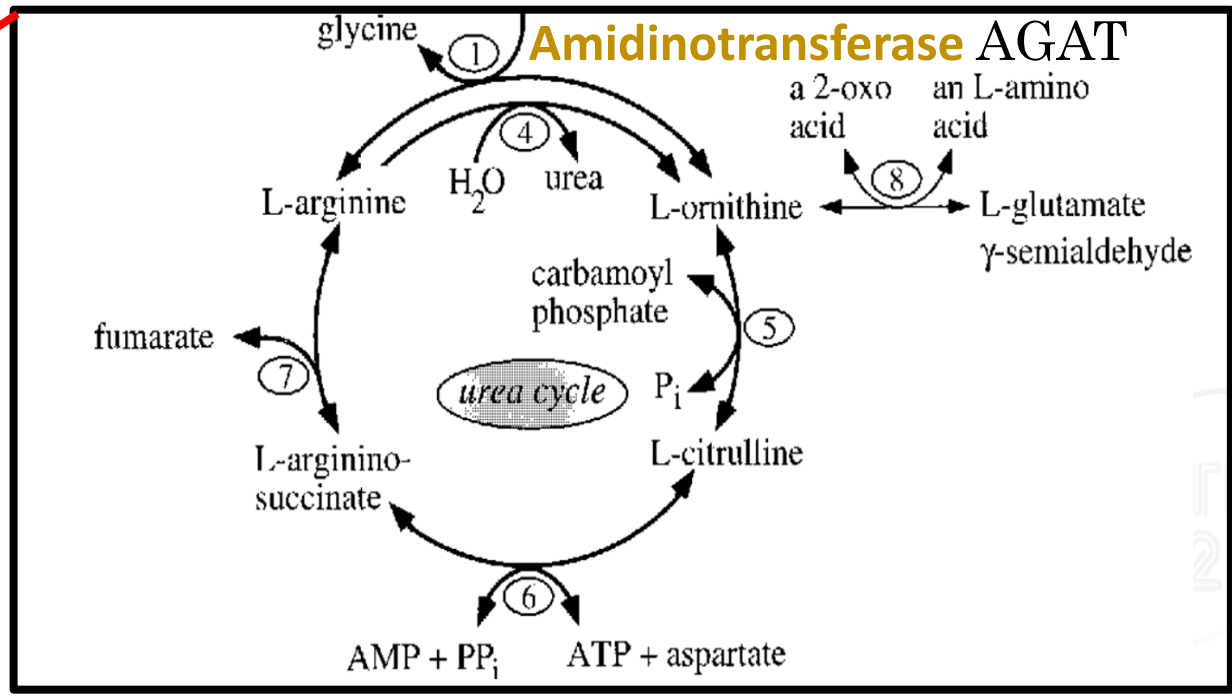


Frontiers in Endocrinology 2022



AAS

1. **Increased muscle mass**
2. **Increases AGAT expression**



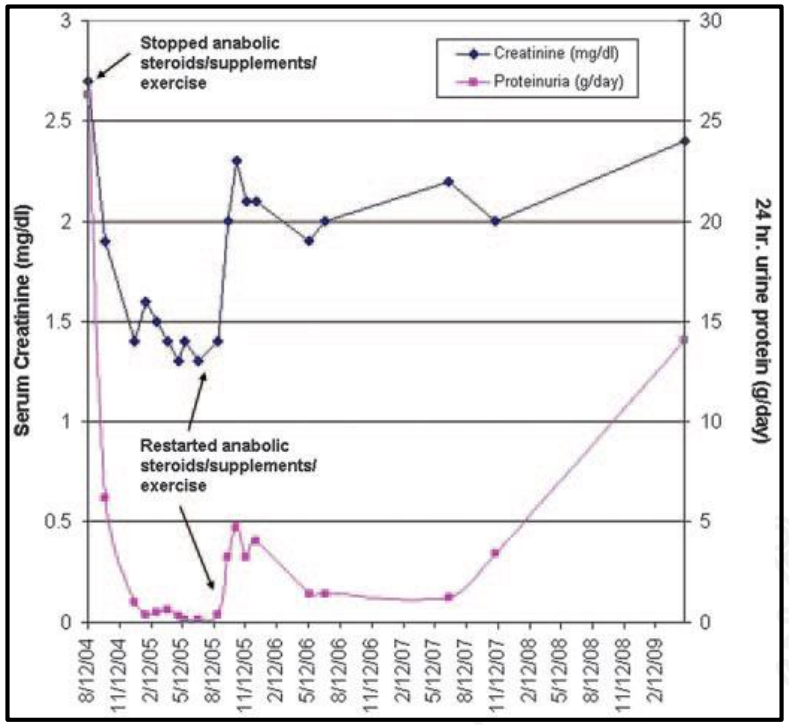
Herlitz et al

Development of Focal Segmental Glomerulosclerosis after Anabolic Steroid Abuse

Table 1. Demographics and clinical history

Patient	Age	Race/ Gender	Height (in)	Weight (kg)	BMI	Exercise	Hormone Use	Supplements/Diet	Hypertension?	Other PMHx
1	30	W/M	71	134	41	Bodybuilding	AASs including M-1-T (testosterone prohormone), GH, and insulin for >10 yr	Creatine, amino acid supplements, glutamate, >550 g/d protein diet	HTN (duration unknown)	Sleep apnea
2	31	W/M	63	102	40	Bodybuilding	AASs including stanzolol and durabolin for 8 yr	High-protein diet (300 to 400 g/d) and protein shakes	HTN for 3 mo	None
3	41	W/M	68	93	31	Bodybuilding	AASs and GH for 20 yr	High-protein shakes	HTN for 5 yr	None
4	28	H/M	66	100	36	Bodybuilding	AASs and GH, "for years"	Creatine for 5 yr	No	None
5	49	W/M	72	114	34	Bodybuilding	AASs "for years"	High-protein diet	No	HIV for 21 yr, on HA undetectable viral load, diabetes
6	38	H/M	71	96	30	Bodybuilding	AASs including sustanon durabolin, primobolan, equipoise, and winstrol "for years"	Unknown	No	None
7	38	H/M	71	107	33	Bodybuilding	AASs and GH for 8 to 10 yr	Creatine, amino acid supplements, 500 g/d protein diet	HTN (duration unknown)	Sleep apnea
8	33	H/M	69	81	27	Bodybuilding	AASs "for years"	High-protein diet	HTN (duration unknown)	None
9	45	W/M	68	130	43	Powerlifting	AASs including testosterone ethanate and deca-durabolin for 15 yr	Amino acid supplements, 300 g/d protein diet	HTN for 18 mo	None
10	40	W/M	67	95	33	Bodybuilding	Intramuscular testosterone injections for "many years"	High-protein diet with 5 protein shakes/d	No	Cocaine use, occasio UTIs

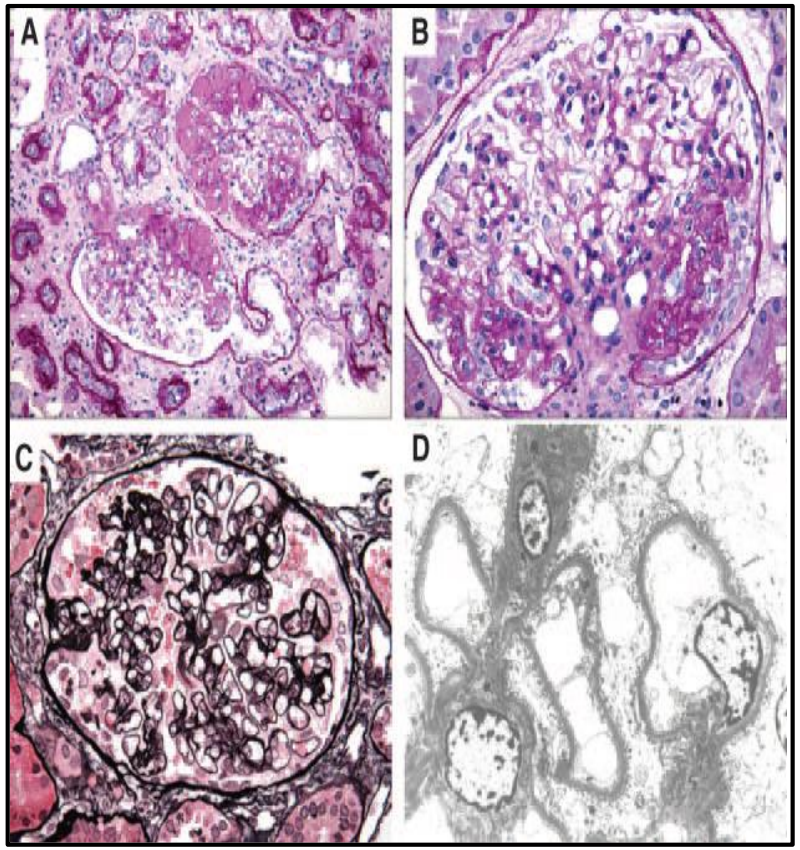
GH, growth hormone; H, Hispanic; HAART, highly active antiretroviral therapy; HTN, hypertension; PMHx, past medical history; UTI, urinary tract infection; W, white.



J Am Soc Nephrol 21: 163–172, 2010

Association of focal segmental glomerulosclerosis and proteinuria in a cohort of 10 bodybuilders

Patient	Light Microscopy					Electron Microscopy
	Pattern	Global Sclerosis	Segmental Sclerosis	TA/IF (%)	Arteriosclerosis	
1	FSGS with collapsing features	16 of 22	4 of 22	80	Mild	95% FPE
2	FSGS, perihilar variant, glomerulomegaly	4 of 17	8 of 17	40	None	90% FPE
3	FSGS NOS	4 of 7	3 of 7	85	Moderate	80% FPE
4	FSGS NOS, glomerulomegaly	4 of 6	1 of 6	60	Mild	NA
5	FSGS NOS, glomerulomegaly	0 of 13	2 of 13	15	Mild	50% FPE
6	Glomerulomegaly	0 of 15	0 of 15	<5	Mild	Moderate FPE, rare intramembranous lucencies
7	FSGS with perihilar lesions, focal cellular and collapsing features	9 of 15	3 of 15	40	Mild to moderate	85% FPE
8	FSGS with perihilar lesions, focal collapsing features	7 of 61	15 of 61	15	Mild	15% FPE
9	FSGS, perihilar variant	5 of 8	2 of 8	60	Moderate	NA
10	FSGS NOS, glomerulomegaly	9 of 17	6 of 17	90	Moderate	90% FPE



J Am Soc Nephrol 21: 163–172, 2010

RESEARCH ARTICLE Open Access

The potential effects of anabolic-androgenic steroids and growth hormone as commonly used sport supplements on the kidney: a systematic review

Dorna Davani-Davari[1], Iman Karimzadeh[1*] and Hossein Khalili[2]

Methods: The search strategy was in accordance with the PRISMA guideline. Seven databases such as Scopus, Medline, Embase, and ISI Web of Knowledge were searched using keywords, such as "growth hormone", "anabolic-androgenic steroids", and "kidney injury". Articles published from 1950 to December 2017 were considered. Randomized clinical trials, prospective or retrospective human studies, case series as well as case reports, and experimental (in vivo) studies were included. Twenty one clinical and experimental articles were selected (12 for anabolic-androgenic steroids and 9 for GH).

38.1% of studies about possible effects of AAS and GH on the kidney were animal investigations.

experimental and clinical studies about the renal safety of AAS (n=12)

Table 1 Summary of experimental and clinical studies about the renal safety of anabolic-androgenic steroids ($n = 12$)

Dose & Duration	Subjects	Type of study	Main results	Reference
50 mg/day dihydrotestosterone intraperitoneally for 10 days	Rats	Experimental	- Increase in blood pressure, and proximal tubule volume reabsorption - Decrease in serum angiotensin II level - No change in glomerular filtration rate	Quan et al. 2004 [29]
500 μg/kg/day testosterone propionate intramuscularly for 2 weeks	Castrated male and oophorectomized female rats with obstructive renal injury	Experimental	Increase in TNF-α production and pro-apoptotic and pro-fibrotic signaling leading to increased apoptotic cell death, tubulointerstitial fibrosis, and renal dysfunction	Metcalfeet al 2008 [28]
0.75 or 2.0 mg/day dihydrotestosterone as subcutaneous implants for 14 weeks	Castrated diabetic male rats	Experimental	- Low doses attenuated castration-associated increases in urine albumin excretion, glomerulosclerosis, and tubulointerstitial fibrosis - High doses exacerbated castration-associated increases in urine albumin excretion, glomerulosclerosis, and tubulointerstitial fibrosis	Xu et al. 2009 [56]
Testosterone implants (20 mg/capsule) changed every 2 weeks	Hypertensive rats on a high sodium diet	Experimental	- Increase in blood pressure & renal sodium reabsorption - Increase in glomerulosclerosis	Liu&Ely 2011 [33]
Single dose of testosterone (12.5 mg/pellet) orally	Female estrogen receptor knockout mice	Experimental	Inducing podocyte apoptosis by androgen receptor activation, independent of the TGF-β1 signaling pathway	Doublier et al. 2011 [48]
Combination of 0.75 mg/day dihydrotestosterone as subcutaneous implants and 0.15 mg/kg/day anastrozole orally for 12 weeks	Diabetic male rats	Experimental	- Attenuating albuminuria, glomerulosclerosis, and tubulointerstitial fibrosis - Decrease in the density of renal cortical CD68-positive cells - Decrease in the expression of transforming growth factor-β, collagen type IV, TNF-α, and IL-6	Manigrasso et al. 2012 [55]
Case 1: Not defined	Case 1: 21-year-old male athlete	Case report and case series	- Arterial hypertension, oliguria, leukocyturia, hematuria and proteinuria, increase in serum urea and creatinine - Moderate interstitial inflammatory infiltrate with eosinophils, interstitial edema, calcium deposits, and mild acute tubular necrosis	Daher et al. 2009 [20]
Case 2: Not defined	Case 2: 30-year-old male bricklayer		- Increase in serum urea and creatinine, hematuria and proteinuria - Mild interstitial lymphmononuclear inflammatory infiltrate with eosinophils without remarkable tubular abnormalities	
Case series: Not defined	Case series: Males & Females aged between 21 and 63 years		- Interstitial nephritis and hypercalcemia secondary to vitamin D intoxication caused acute kidney injury	
At least one anabolic steroid (e.g., testosterone 500 mg twice weekly) intramuscularly for several months	10 body builders aged between 28 and 49 years	Case series	- Proteinuria, renal insufficiency, and nephrotic syndrome - Focal segmental glomerulosclerosis, tubular atrophy, and interstitial fibrosis	Herlitz et al. 2010 [57]
Not defined	38-year-old man	Case report	- High serum creatinine, high serum urea, low hemoglobin level - Intrinsic renal parenchymal and focal segmental glomerulosclerosis	Harrington et al. 2011 [58]
- Nandrolone intramuscular injection 400 mg twice per week for 6 weeks - Testosterone intramuscular injection 400 mg once per week for 6 weeks	41-year-old male bodybuilder	Case report	Acute kidney injury with the pathology of diffuse acute tubular injury due to bile acid nephropathy with the pathology of tubular bile acid casts	Luciano et al. 2014 [19]
Case 1: Stanozolol intramuscular injection 10 mg three times per week for 5 weeks Case 2: Stanozolol intramuscular injection 1 mg three times per week for 6 weeks	Case 1: 30-year-old male amateur bodybuilder Case 2: 43-year-old male amateur bodybuilder	Case report	Bile cast nephropathy due to cholestatic jaundice characterized by acute tubular epithelial cell damage along with increased serum creatinine and oliguria	Tabatabaee et al. 2015 [23]
Oxandrolone, boldenone undecyclenate, stanozolol, and trenabol (with not-defined daily dose and duration of treatment)	28-year-old male bodybuilder	Case report	Acute kidney injury in the setting of severe cholestatic jaundice with the pathology of bile inclusions within tubular cells and interstitial edema	Alkhunaizi et al. 2016 [24]

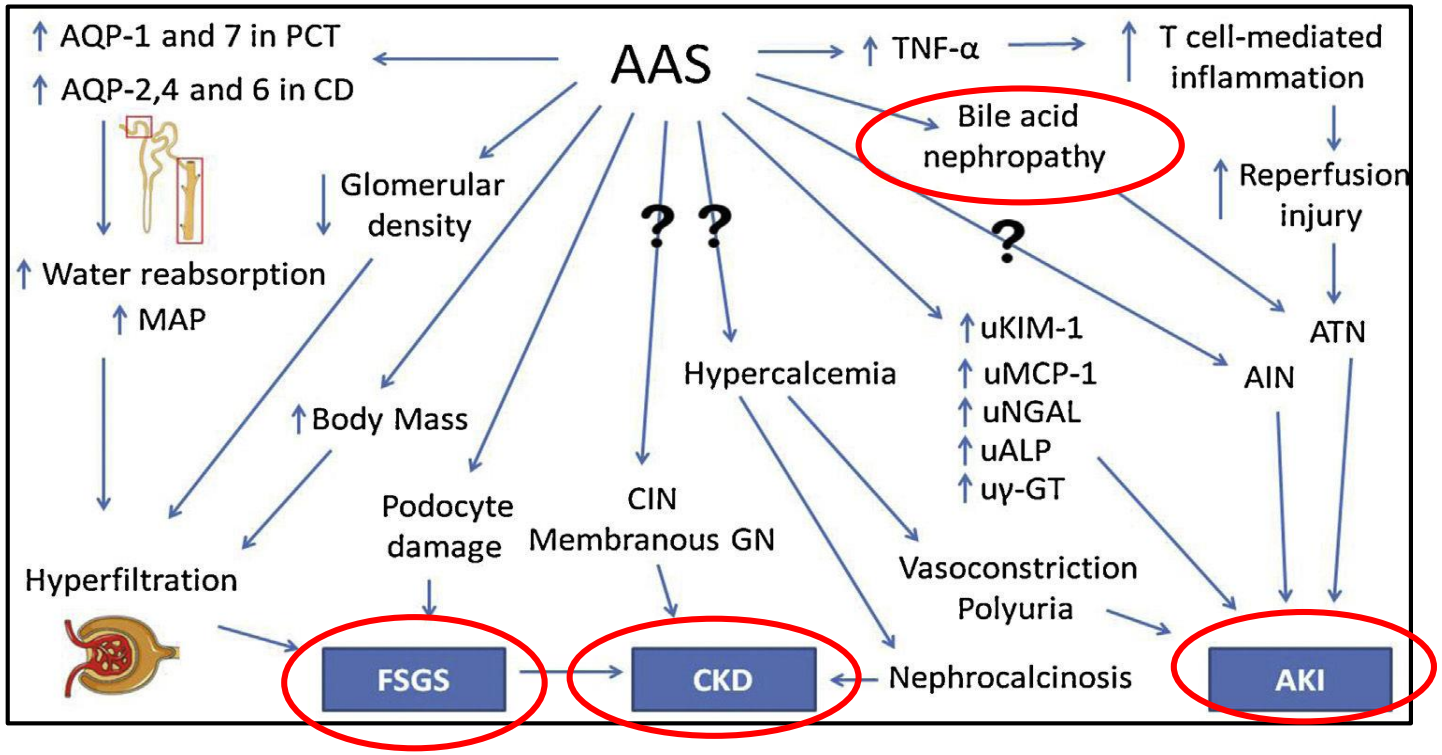
experimental and clinical studies about the renal safety of growth hormone (n=9)

Table 2 Summary of experimental and clinical studies about the renal safety of growth hormone ($n = 9$)

Dose & Duration	Subjects	Type of study	Main results	Reference
2.5, 5, 10, and 20 IU/kg/day subcutaneously for 4–60 days	Female rats	Experimental	- Dose-dependent increase in renal weight - No change in kidney dry weight/ body weight ratio - Increase in renal glomerular and tubular cell proliferation and renal DNA/protein ratio	Mehls et al. 1993 [86]
0.025, 0.1, and 1 IU/kg/day subcutaneously for 14 weeks	Male and female dogs	Experimental	- Increase in body weight gain and kidney weights - Glomerular deposits, mesangial thickening, and very slight cellular infiltration in glomeruli - Increase in the renal glomerular area - Glomerular basal lamina thickening - Increase in mesangial matrix	Molon-Noblot et al. 2000 [87]
5–10 mg/day for 3–9 days	2 patients with hypopituitarism, 1 with cirrhosis of the liver and 2 with chronic nephritis and uremia	Case report	- Decrease in plasma urea level and urea excretion - Prompt increase in creatinine clearance and phosphorus reabsorption	Gershberg 1960 [80]
More than 400 mg/week testosterone proprionate and/or nandrolone deconate intramuscularly	4 body builders aged between 20 and 26 years	Case report	- Increase in serum creatinine and decreased in eGFR - Development of acute tubular necrosis	Almukhtar et al. 2015 [22]
50 ng/kg/min as an infusion for 2 h	Healthy men	Pilot clinical trial	- Decrease in renal plasma flow - No change in GFR	Parving et al. 1978 [81]
2 IU in the morning and 4 IU in the evening subcutaneously for 1 week	Healthy men	Pilot clinical trial	- Increase in GFR and renal plasma flow - No significant change in kidney size and urinary excretion rates of albumin and β2-microglobulin	Christiansen et al. 1981 [93]
0.125 IU/kg per week subcutaneously for the first 4 weeks and 0.25 IU/kg per week for the subsequent 5 months	Growth hormone deficient adults	Double-blind, placebo-controlled cross-over clinical trial	- No change in GFR and renal plasma flow - No effect on kidney size	Riedl et al. 1995 [82]
0-02 IU/kg/day (or 7 μg/kg/day) subcutaneously for 10 months	Adults with childhood onset GH deficiency	Pilot clinical trial	- Increase in left ventricular-mass index and kidney length - No abnormalities or change in the urine analysis	Link et al. 2001 [94]
6 IU/m^2 per day subcutaneously for 6 days	Healthy volunteer males	Randomized, cross-over clinical trial	- Increase in the plasma renin - Increase in distal tubule sodium and water reabsorption - Decrease in mean 24-h urinary output and mean 24-h urinary sodium excretion	Hansen et al. 2001 [99]

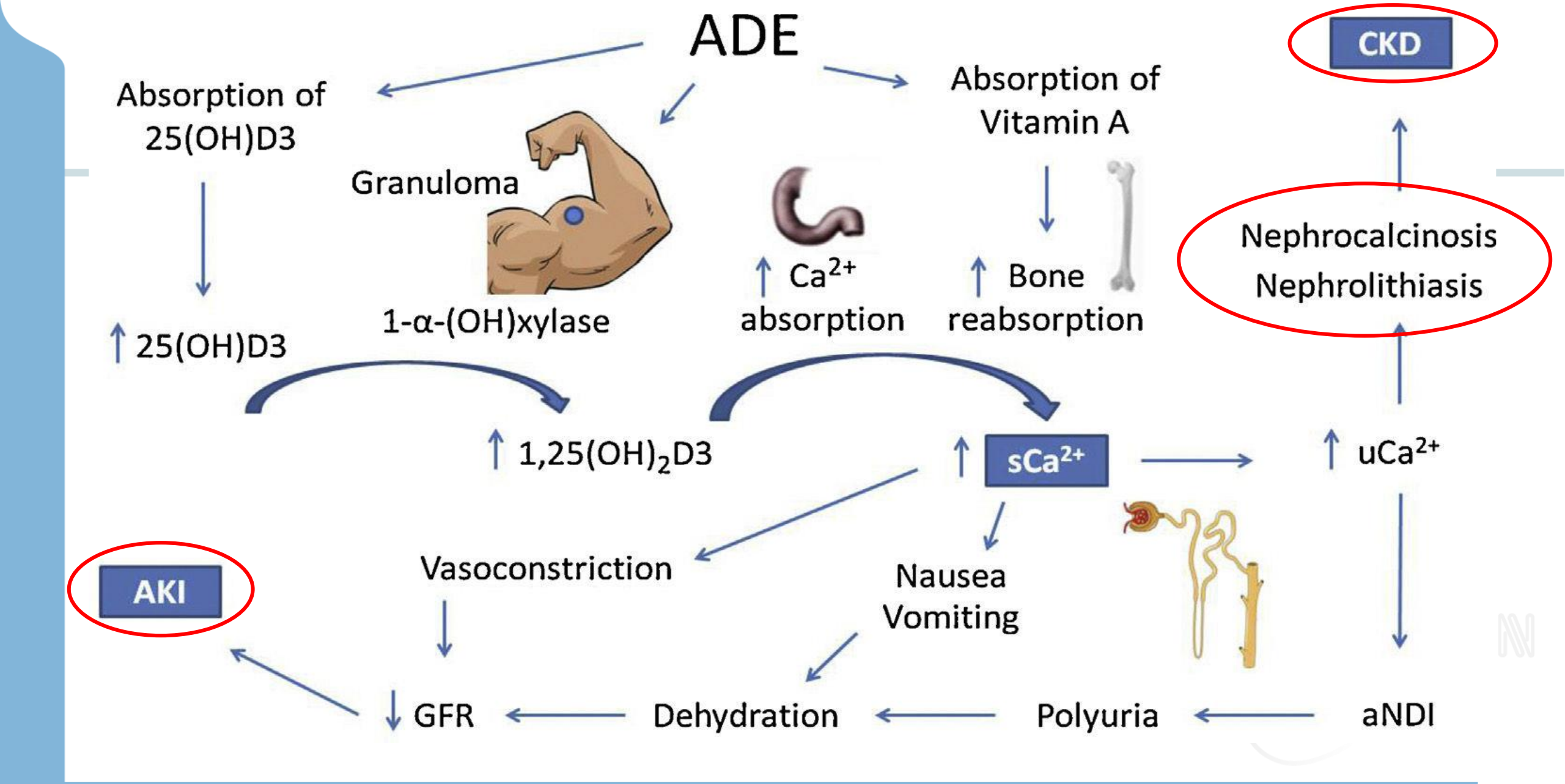
Evidence regarding adverse effects of **anabolic-androgenic steroids** on kidney exists;
AKI
CKD
FSGS

GH's exact effect on the kidney at doses used by athletes and body builders has not yet been clarified.



All major sports organizations have banned AAS use

- ✓Creatine
- ✓Protein
- ✓Anabolic androgenic steroids / GH
- ✓**vitamins**


ADE
Absorption of 25(OH)D3
Granuloma
Absorption of Vitamin A
CKD
Nephrocalcinosis
Nephrolithiasis
↑ 25(OH)D3
1-α-(OH)xylase
↑ Ca2+ absorption
↑ Bone reabsorption
↑ 1,25(OH)2D3
↑ sCa2+
↑ uCa2+
AKI
Vasoconstriction
Nausea
Vomiting
↓ GFR
Dehydration
Polyuria
aNDI

International Journal of
Environmental Research and Public Health

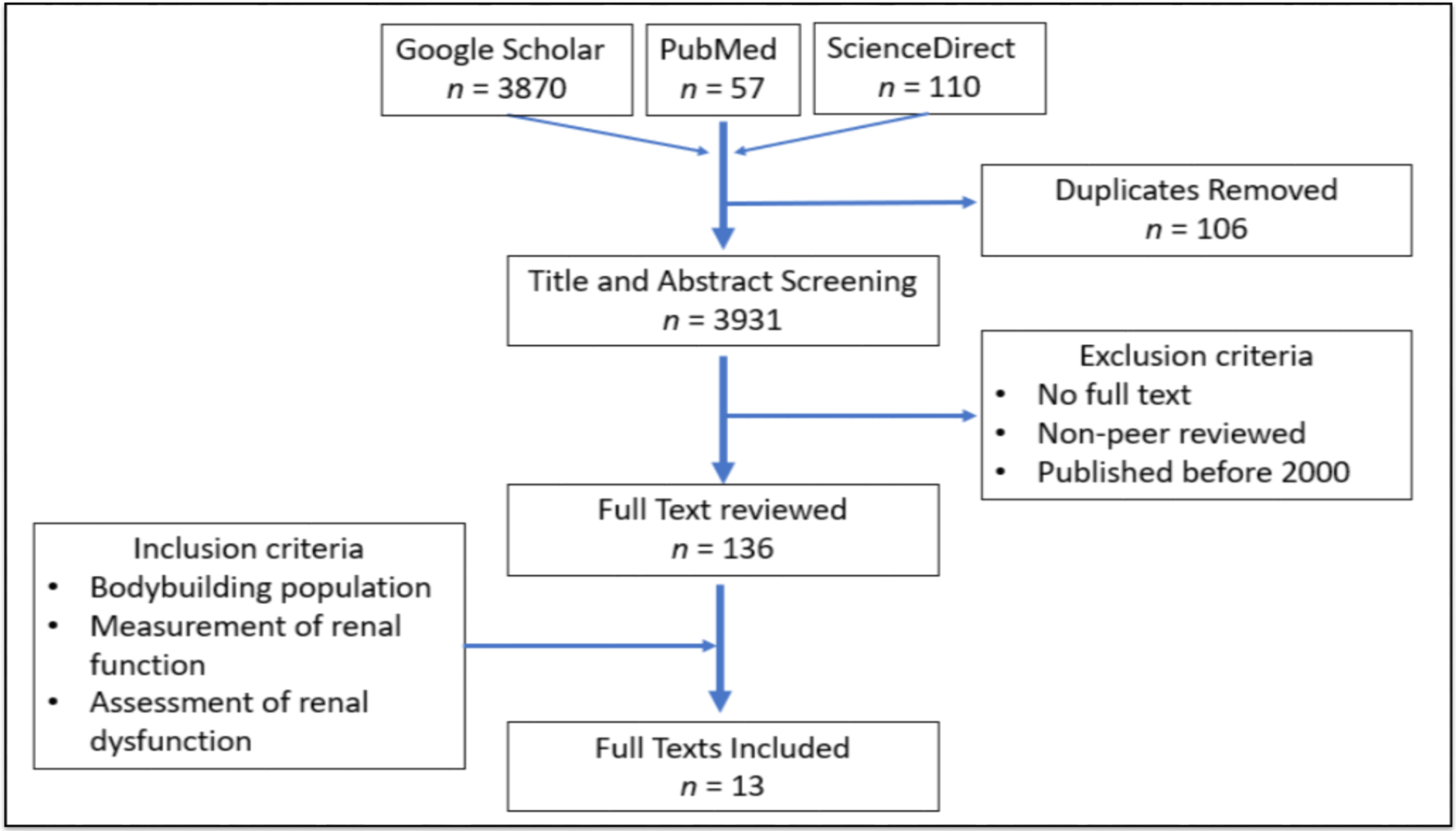
MDPI

Review

Nutritional and Non-Nutritional Strategies in Bodybuilding: Impact on Kidney Function

Victoria Tidmas [1], Jon Brazier [1,*], Janine Hawkins [2], Scott C. Forbes [3], Lindsay Bottoms [1] and Ken Farrington [2,4]

3 April 2022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n = 3931
Exclusion criteria
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• Non-peer reviewed
• Published before 2000
Full Text reviewed
n = 136
Inclusion criteria
• Bodybuilding population
• Measurement of renal function
• Assessment of renal dysfunction
Full Texts Included
n = 13

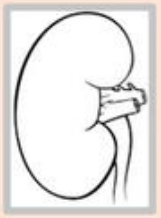
Background

Bodybuilding (BB) is popular recreationally & competitively. Extreme training and dietary regimes are used to achieve muscular definition and symmetry.

→ **97%** of **BB** utilise supplements →

Increased concern of effect on health, particularly on the **Kidneys**

13 articles relating to **Bodybuilding and Kidney Disease**



Acute interstitial nephritis
Acute tubular necrosis
Focal segmental glomerulosclerosis (FSGS)
Nephrocalcinosis
Chronic Interstitial Nephritis

- **Acute Kidney Injury (AKI)**
- **Chronic Kidney Disease (CKD)**
- **End Stage Kidney Disease (ESKD)**

	 **Protein**	 **Creatine**	 **Anabolic androgenic steroids**	 **Vitamins A, D, E**	 **NSAID and Diuretics**
	2 – 5 g/kg/day	Loading 20g/day Maintenance 5 g/day	Up to 250mg/day testosterone	Up to 20 times the recommended for livestock	Not specified
	⬆ Hyperfiltration ⬆ Renal decline	Prolonged & High intake = **Safe**	⬆ AKI ⬆ Later presentation ⬆ Severity ⬆ FSGS	⬆ AKI & CKD ⬆ Hypercalcaemia ⬆ Nephrocalcinosis	⬆ AKI & CKD

Conclusion

High Protein, Creatine
Anabolic Androgenic Steroids
Vitamins
NSAID, Diuretics

→ **Increase risk** of developing **AKI, CKD, & ESKD**

Multiple concurrent practices. Inaccurate measure of intakes. Training phase not specified. Little attempt to detect subclinical disease →

Research needed to isolate effects of supplements and define risks

1-Which organ doesn’t play role in creatine production ?

a-liver

b-kidney

c-pancreas

d-muscle

2-Which protein doesn't increase GFR?

a-white egg

b-fish

c-soy

d-beef

THANKS FOR YOUR KIND ATTENTION