Epidemiologija akutnog i kroničnog bubrežnog zatajenja u onkoloških bolesnika

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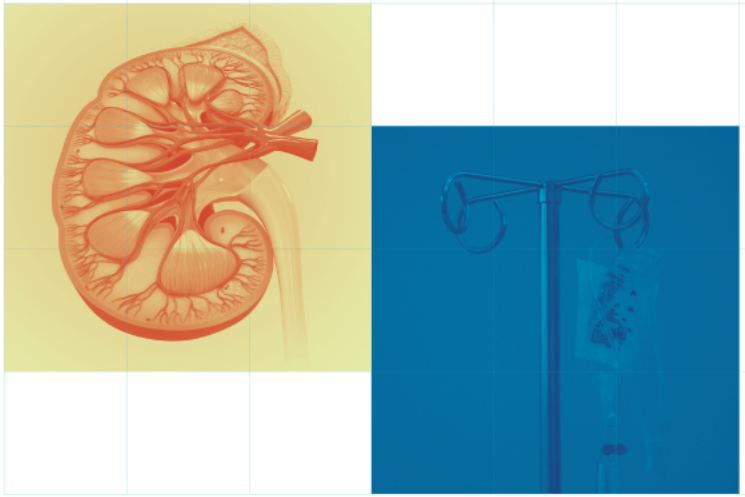
Nefrolog; KB Dubrava



Zajednički simpozij Hrvatskog društva za internističku onkologiju i Hrvatskog društva za nefrologiju, dijalizu i transplantaciju Hrvatskog liječničkog zbora

8.2.2020.

Hrvatski liječnički zbor, Zagreb

HDIO

Hrvatsko društvo za nefrologiju, dijalizu i transplantaciju Hrvatskog liječničkog zbora

Akutno bubrežno oštećenje (eng. AKI – Acute kidney injurie)

Table 1 | **Diagnosis and staging of AKI**

Stage[a]	Serum creatinine level	Urine output
Diagnosis	• Increase of ≥0.3 mg/dl (26.5 µmol/l) within 48 h, or • Increase of ≥1.5-fold above baseline, known or assumed to have occurred within 7 days	• <0.5 ml/kg/h for 6 h
1	• ≥1.5–1.9 times baseline, or • >0.3 mg/dl (26.5 µmol/l) increase from baseline	• <0.5 ml/kg/h for 6–12 h
2	• ≥2.0–2.9 times baseline	• <0.5 ml/kg/h for ≥12 h
3	• ≥3.0 times baseline, or • Increase of serum creatinine to ≥4.0 mg/dl (353.6 µmol/l), or • RRT or • In patients aged <18 years, a decrease in eGFR to <35 ml/min/1.73 m^2	• <0.3 ml/kg/h for ≥24 h or • Anuria for ≥12 h

Hoste et al; Nature reviews; 2018;
KDIGO AKI guidelines: 2012.

AKI staging		RIFLE	
Serum creatinine	Urine output (common to both)	Class	Serum creatinine or GFR
Stage 1 Increase of more than or equal to 0.3 mg/dl (⩾26.5 μmol/l) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg/h for more than 6 hours	Risk	Increase in serum creatinine × 1.5 or GFR decrease >25%
Stage 2 Increased to more than 200% to 300% (>2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours	Injury	Serum creatinine × 2 or GFR decreased >50%
Stage 3 Increased to more than 300% (>3-fold) from baseline, or more than or equal to 4.0 mg/dl (⩾354 μmol/l) with an acute increase of at least 0.5 mg/dl (44 μmol/l) or on RRT	Less than 0.3 ml/kg/h for 24 hours or anuria for 12 hours	Failure	Serum creatinine × 3, or serum creatinine >4 mg/dl (>354 μmol/l) with an acute rise >0.5 mg/dl (>44 μmol/l) or GFR decreased >75%
		Loss	Persistent acute renal failure=complete loss of kidney function >4 weeks
		End-stage kidney disease	ESRD >3 months

KDIGO AKI guidelines; 2012.

Injury

Up to 7 days → 7–90 days → >90 days

AKI KDIGO stage	AKD stage (congruent to AKI stage)
Ongoing RRT	Ongoing RRT
3 (SCr 3×baseline) and/or RRT	3 (SCr 3×baseline) and/or RRT
2 (SCr 2×baseline)	2 (SCr 2×baseline)
1 (SCr 1.5×baseline)	1 (SCr 1.5×baseline)
Subacute AKI	0 Subacute AKI

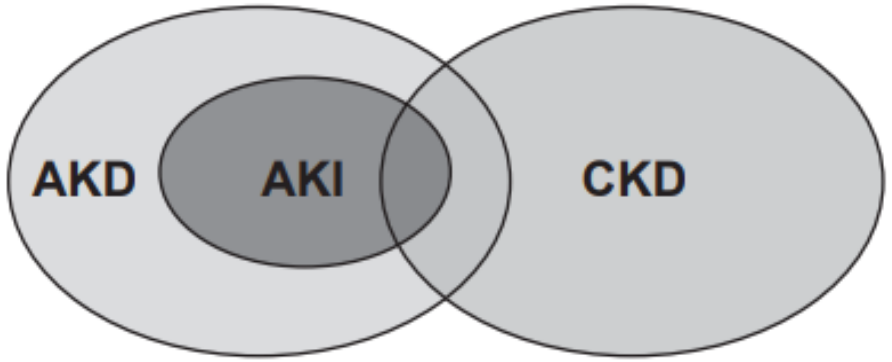
→ CKD

Stage 0 subtypes

C: SCr not back to baseline

B: Elevated biomarker levels or loss of renal reserve indicates injury

A: No evidence of injury



Hoste et al; Nature reviews; 2018;
KDIGO AKI guidelines: 2012.

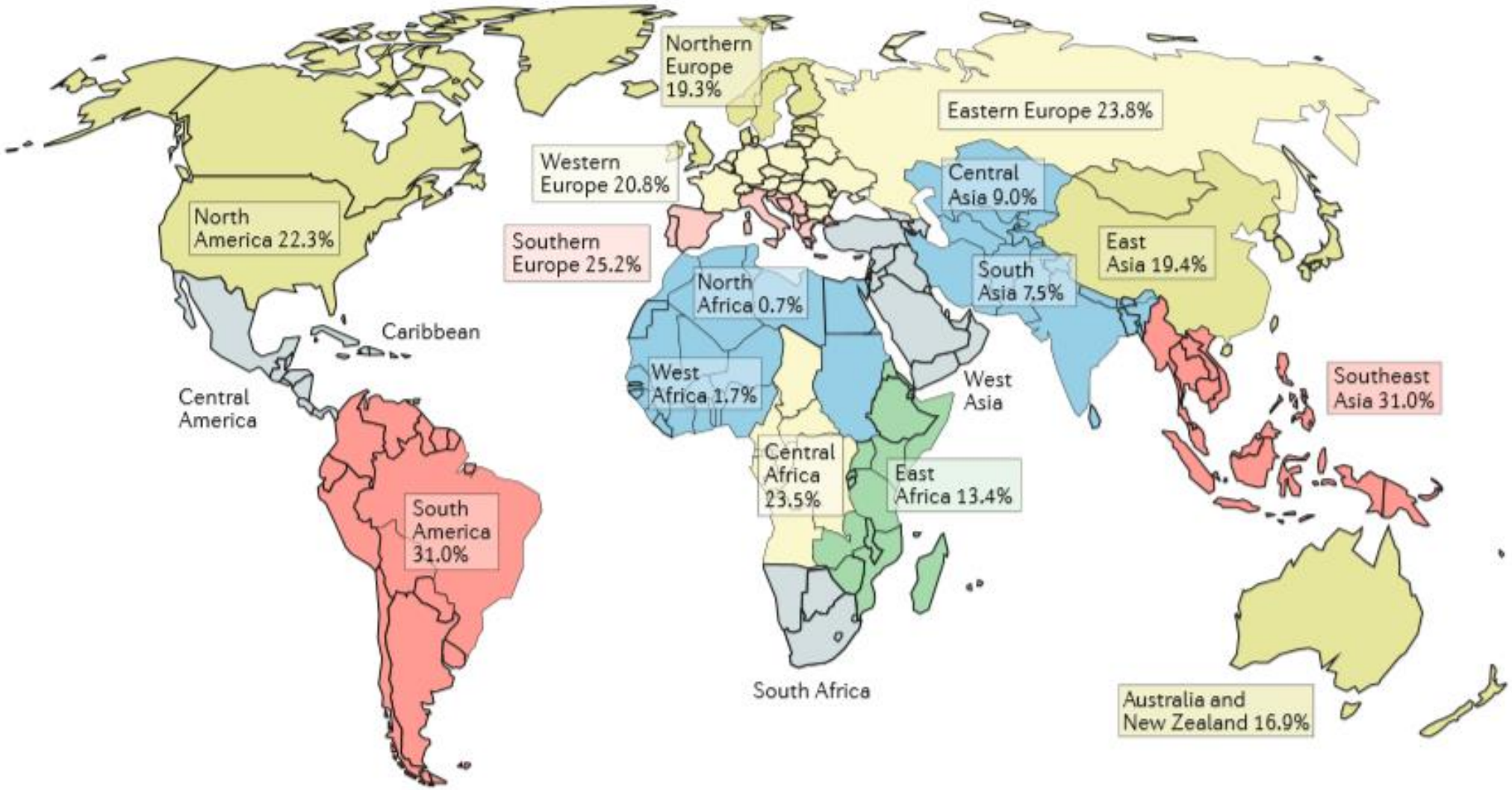


Fig. 3 | **Global variation in the incidence of AKI.** Published estimates of the incidence of acute kidney injury (AKI) as defined using Kidney Disease: Improving Global Outcomes (KDIGO) criteria vary widely across countries and regions. The percentages shown represent the proportion of the hospitalized population with AKI. Data from REFS[3,20].

Hoste et al; Nature reviews; 2018;

Epidemiologija i ishodi u bolesnika s AKI – rezultati više kohorti

Populacija	Dob	Incidencija (raspon)	Potreba za dijalizom (%)	Smrtnost (%)
Hospitalizirani pacijenti (izvan JIL)	Odrasli	<1 na 5 bolesnika	<10	10 do 20
Teški bolesnici (JIL)	Odrasli	1 na 3 do 2 na 3 bolesnika	5 do 11	N/A
	Djeca	1 na 4 bolesnika (10-82%)	1 do 2	11
Bolesnici nakon kardiokirurškog liječenja	Odrasli	1 na 5 bolesnika (2-50%)	<5	10
	Djeca	1 na 3 do 1 na 2 bolesnika	N/A	6
Bolesnici sa sepsom	Odrasli	1 na 20 do 1 na 2 bolesnika	15	30 do 60

Epidemiološke razlike u AKI

Uz bolesnika vezani čimbenici

Dob, spol, etnicitet

Komorbiditeti: Šećerna bolest, KV bolesti, KBB

Kronična terapija: NSAR, ACE inhibitori, diuretici

Čimbenici vezani uz akutnu bolest

Vrsta i težine bolesti koj je dovela do AKI: septični šok, kardiogeni šok

Izloženost nefrotoksičnim lijekovima i tvarima: aminoglikozidi, diuretici, kontrastna sredstva

Oštećenja organa/organskih sustava

Čimbenici vezani uz dijagnostičke kriterije

Varijanta dijagnostičkog krterija: KDIGO, RIFLE, AKIN

Korištenje samo vrijednosti serumskog kreatinina

Razlike u kriterijima/procjeni diureze

Odustnost početnih/recentnih vrijednosti serumskog kreatinina

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Table 3 | **The contrasting characteristics of AKI around the world**

Characteristic	High-income countries[a]	Low-to-middle income countries[b]
Pattern of occurrence	Occurs predominantly in ICUs	Occurs in rural health centres and hospitals as well as in large urban hospitals
Disease patterns	Associated with multiple organ failure	Often caused by a single disease; multiple organ failure is uncommon
Mortality	High mortality	Mortality similar to or even higher than in high-income countries
Demographics	A disease of elderly populations	A disease of otherwise healthy children and young persons
Incidence	Increasing	Increasingly recognized as high
Reporting	Adequately reported	Severely under-reported
Prevention	Difficult to prevent	Preventable, generally with public health initiatives
Cost	Very expensive to treat	Very inexpensive to treat at early stages; unaffordable at severe stages
Main exposures	• Sepsis and septic shock • Trauma • Complex surgery (cardiac surgery or major non-cardiac surgery) • Nephrotoxic drugs and agents • Burns	• Diarrhoea and endemic infections: malaria, leptospirosis, dengue fever, cholera, yellow fever, tetanus, hantavirus and HIV/AIDS • Obstetric complications (including septic abortion) • Animal venoms (snakes, bees and wasps, *Loxosceles* spp. spiders and *Lonomia* spp. caterpillars) • Natural and traditional remedies and natural dyes • Prolonged physically demanding work in an unhealthy environment

ICU, intensive care unit. [a]Includes World Bank upper-middle income (US$3,956–12,235) and high-income (>US$12,236) categories. [b]Includes World Bank low-income (<US$1,005) and lower-middle income (US$1,006–3,955) categories[7].

Hoste et al; Nature reviews; 2018;

Rizik za AKI u onkoloških bolesnika

- Danska: populacijska studija; period 1999-2006; 37,267 bolesnika
- Rizik za AKI definiran porastom SCr za >50% u odnosu na SCr unutar godine dana od dijagnoze tumorske bolesti
- Jednogodišnji rizik 17,5%, petogodišnji 27%
- Rizik je bio najveći u bolesnika s karcinomima: bubrega (44%), jetre (33%) i multiplog mijeloma (32%)
- Nadomještanje bubrežne funkcije u 5,1% bolesnika unutar jedne godine od episode AKI

Christiansen CF, Johansen MB, Langeberg WJ, et al. Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. Eur J Intern Med 2011; 22:399.

- Ontario, Kanada; period 2007-2014; 163,071 onkoloških bolesnika; kemoterapija;
- 1 od 10 hospitaliziran zbog AKI ili potrebe za dijaliznim liječenjem
- Godišnja incidencija AKI u porastu s 18 na 52 na 1000 bolesnika po godini u period praćenja
- Malignomi s najvećom petogodišnjom incidencijom AKI: multipli mijelom (26%), karcinom mokraćnog mjehura (19%), leukemije (14%)
- Čimbenici povećanog rizika: uznapredovalost maligne bolesti, KBB, šećerna bolest;
- Rizik naznačen unutar 90 dana od primjene sistemne terapije

Kitchlu A, McArthur E, Amir E, et al. Acute Kidney Injury in Patients Receiving Systemic Treatment for Cancer: A Population-Based Cohort Study. J Natl Cancer Inst 2018.

- Rizik za AKI je veći u:
  - onkoloških bolesnika koji su bili u JIL, onih
  - koji s liječeni zbog visokorizičnog mijelodisplastičnog sindroma ili akutne leukemije
  - bolesnika liječenih transplantacijom hematopoetskih matičnih stanica
  - nefrektomiranih zbog carcinoma.

Hu SL, Chang A, Perazella MA, et al. The Nephrologist's Tumor: Basic Biology and Management of Renal Cell Carcinoma. J Am Soc Nephrol 2016; 27:2227.

Cho A, Lee JE, Kwon GY, et al. Post-operative acute kidney injury in patients with renal cell carcinoma is a potent risk factor for new-onset chronic kidney disease after radical nephrectomy. Nephrol Dial Transplant 2011;

Libório AB, Abreu KL, Silva GB Jr, et al. Predicting hospital mortality in critically ill cancer patients according to acute kidney injury severity. Oncology 2011; 80:160.
Darmon M, Ciroldi M, Thiery G, et al. Clinical review: specific aspects of acute renal failure in cancer patients. Crit Care 2006; 10:211.
Lahoti A, Kantarjian H, Salahudeen AK, et al. Predictors and outcome of acute kidney injury in patients with acute myelogenous leukemia or high-risk myelodysplastic syndrome. Cancer 2010; 116:4063.

- Većina opservacijskh studija: onkološki bolesici koji razviju AKI i/ili su liječeni dijaliznim metodama imaju povećanu smrtnost
- Studija: Brazil, 288 onkoloških bolesnika, onkološki JIL;
- RIFLE stupnjevi:
  - Risk 49% smrtnosti
  - Injurie 62% smrtnosti
  - Failure 87% smrtnosti
- Onkološki pacijenti bez AKI: 14% smrtnosti u JIL

Benoit DD, Hoste EA. Acute kidney injury in critically ill patients with cancer. Crit Care Clin 2010; 26:151.
Darmon M, Thiery G, Ciroldi M, et al. Intensive care in patients with newly diagnosed malignancies and a need for cancer chemotherapy. Crit Care Med 2005; 33:2488.
Soares M, Salluh JI, Carvalho MS, et al. Prognosis of critically ill patients with cancer and acute renal dysfunction. J Clin Oncol 2006; 24:4003.

Libório AB, Abreu KL, Silva GB Jr, et al. Predicting hospital mortality in critically ill cancer patients according to acute kidney injury severity. Oncology 2011; 80:160.

- Finnish Cancer Registry;
- 13,860 bolesnika – 5 godina nakon dijagnoze
- Mlađi od 35 godina
- nefritis (HR 1.9, 95% CI 1.5–2.2)
- kidney failure (HR 3.6, 95% CI 2.4–5.3)

Liuhto, N., Grönroos, M. H., Malila, N., Madanat-Harjuoja, L., Matomäki, J., & Lähteenmäki, P. (2019). *Diseases of renal function and bone metabolism following treatment for early-onset cancer: A registry-based study. International Journal of Cancer.* doi:10.1002/ijc.32687

- Childhood Cancer Survivor Study Cohort:
  - RR za gr 1-4 : 1.5 (95% CI 1.3-1.8),
  - RR za gr 3-4 KBB 8.1 (95% CI 2.9-23.1)
- Bonnesen et al.:
  - RR 2,5 za bilo koju bubrežnu bolest/oštećenje
  - Nordic register data
  - 32,519 bolesnika (prva godina preživljenja: djeca)
  - RR 2.5 za nefrotski sindrom
  - RR 7.5 i 5.4 za AKI tj KBB

Kronična bubrežna bolest

- Poremećaj bubrežne funkcije > 3 mjeseca
- KBB vs biološko starenje bubrega

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				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
	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			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

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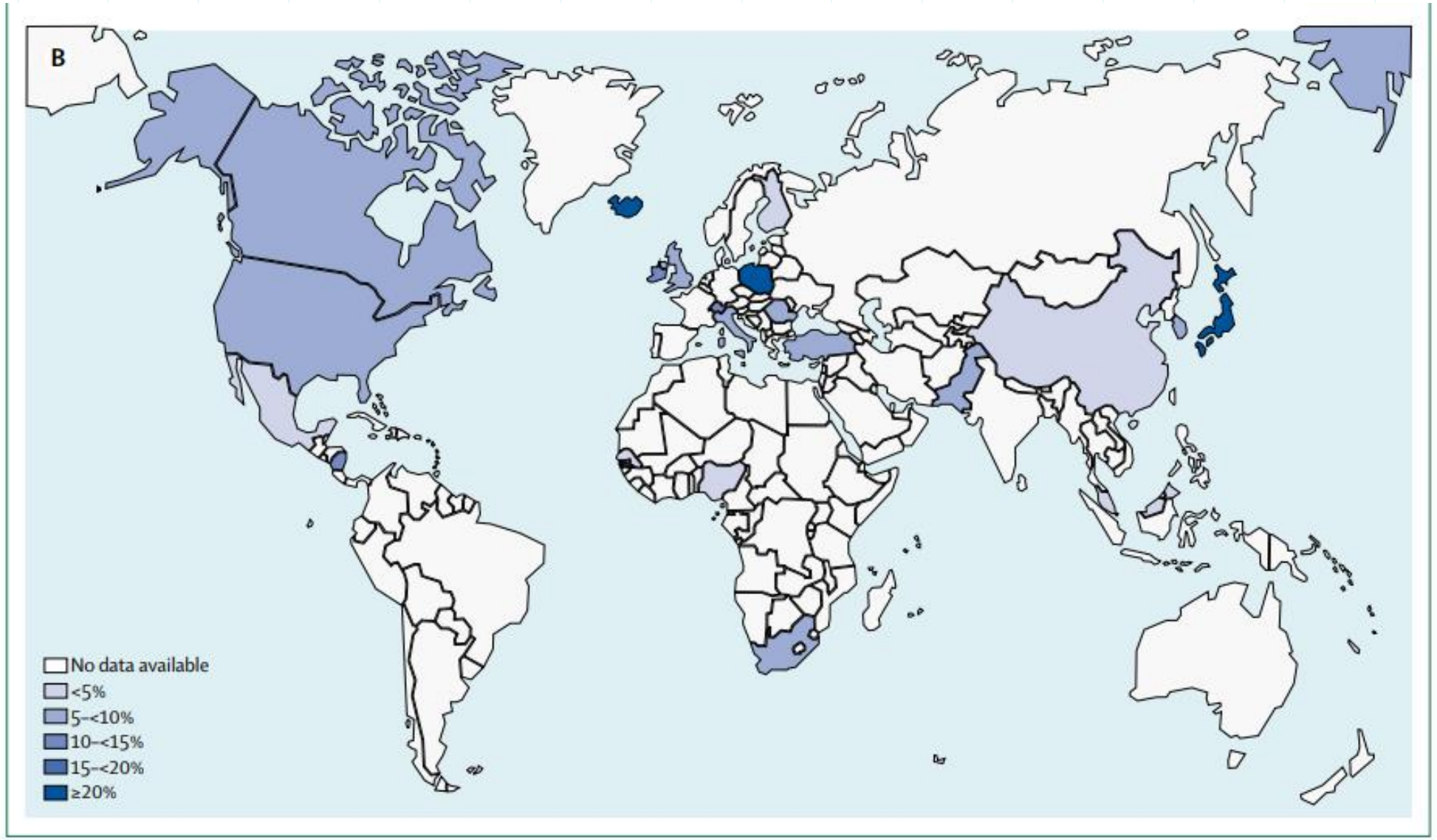
KDIGO CKD, 2012



Hrvatsko društvo za nefrologiju, dijalizu i transplantaciju Hrvatskog liječničkog zbora

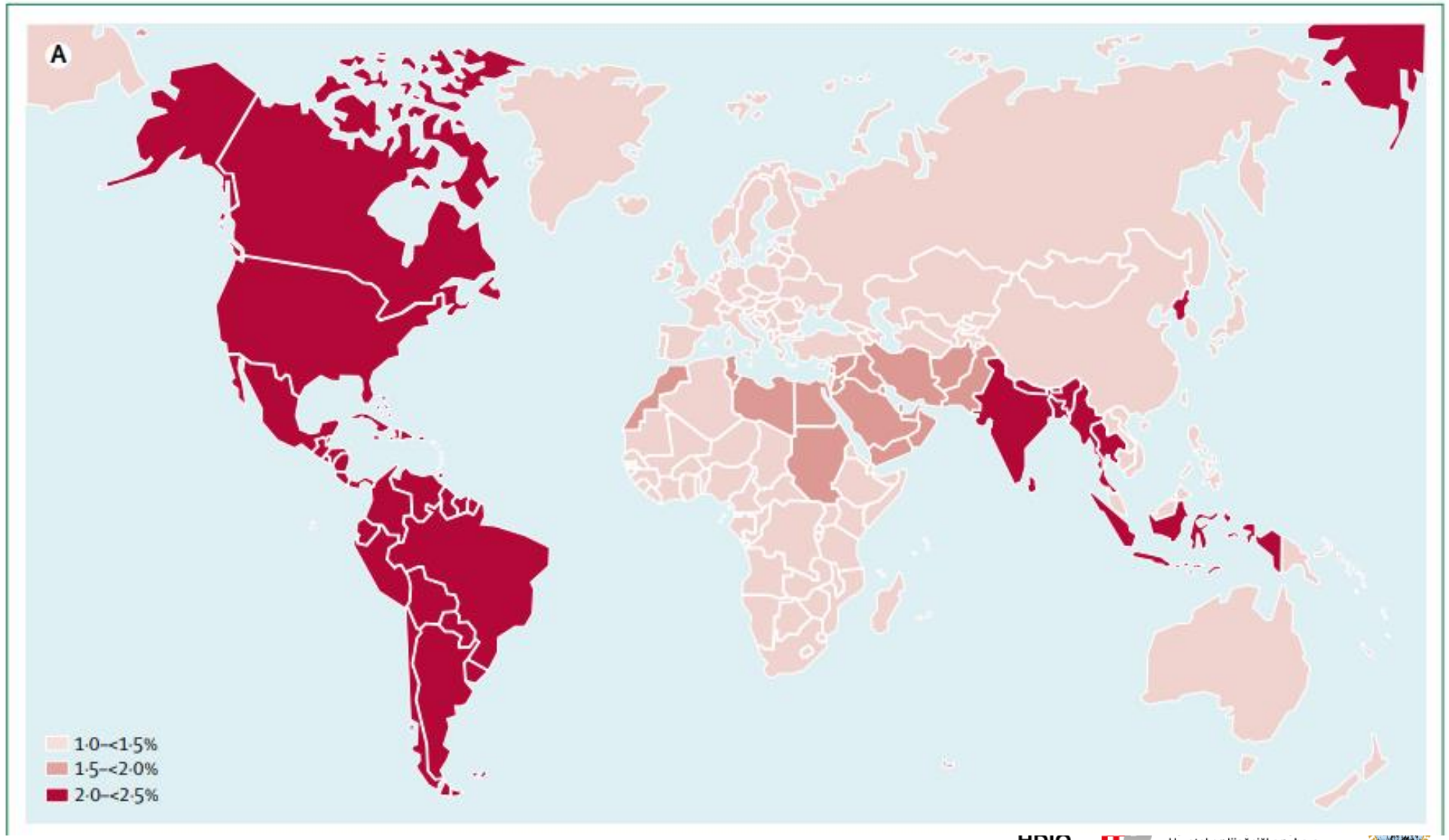
Webster AC, Lancet, 2017

Table 1. Mean prevalence of CKD split by geographical region with 95% Confidence Intervals.

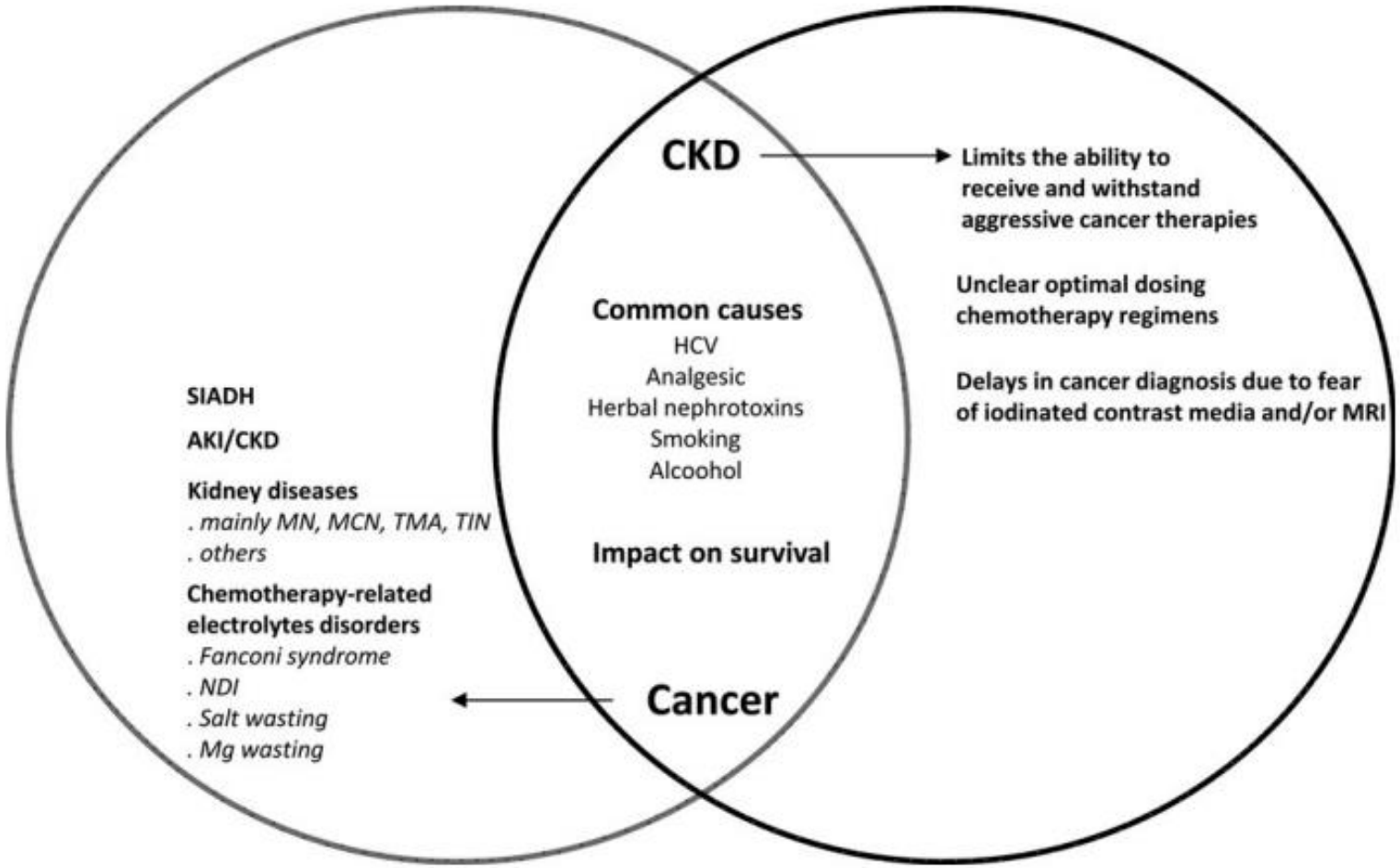
	Stage 1 to 5		Stages 3 to 5	
	N*	Prevalence (%)	N*	Prevalence (%)
S Africa, Senegal, Congo	5,497	8.66 (1.31, 16.01)	1,202	7.60 (6.10, 9.10)
India, Bangladesh	1,000	13.10 (11.01, 15.19)	12,752	6.76 (3.68, 9.85)
Iran	17,911	17.95 (7.37, 28.53)	20,867	11.68 (4.51, 18.84)
Chile	0	NONE	27,894	12.10 (11.72, 12.48)
China, Taiwan, Mongolia	570,187	13.18 (12.07, 14.30)	62,062	10.06 (6.63, 13.49)
Japan, S Korea, Oceania	654,832	13.74 (10.75, 16.72)	298,000	11.73 (5.36, 18.10)
Australia	12,107	14.71 (11.71, 17.71)	896,941	8.14 (4.48, 11.79)
USA, Canada	20,352	15.45 (11.71, 19.20)	1,319,003	14.44 (8.52, 20.36)
Europe	821,902	18.38 (11.57, 25.20)	2,169,183	11.86 (9.93, 13.79)

Hill N et al, PLOS ONE, 2016

Mortalitete povezan uz KBB



Webster AC, Lancet, 2017



Hrvatsko društvo za nefrologiju, dijalizu i transplantaciju Hrvatskog liječničkog zbora

Izzedine et al, NDT 2015

KBB u onkoloških bolesnika

- Česta komplikacija malignih bolesti/onkološkog liječenja
- visoka prevalencija KBB u bolesnika s raznim malignomima
- IRMA i IRMA follow up (2007 i 2010): 2 studije, oko 5000 bolesnika; oko 50% bolesnika s aktivnim malignomom imalo je GFR of <90 mL/min/1.73 m2
- Prevalencija stupnja 3 KBB iznosilo je 12% odnosno 1% stupnja 4 KBB

Launay-Vacher V, Oudard S, Janus N, et al. Prevalence of Renal Insufficiency in cancer patients and implications for anticancer drug management: the renal insufficiency and anticancer medications (IRMA) study. Cancer 2007; 110:1376.
Launay-Vacher V. Epidemiology of chronic kidney disease in cancer patients: lessons from the IRMA study group. Semin Nephrol 2010; 30:548.

KBB u onkoloških bolesnika

- Iff S i sur.; prospektivna studija; 4077 bolesnika; različite maligne bolesti:
  - 30% je imalo eGFR of <60 mL/min/1.73 m2
  - 8.3% je imalo eGFR of 45 mL/min/1.73 m2

- Slični postotci u studijama Na SY (2011) na 8,223 bolesnika i Königsbrügge O (2014) na 1100 bolesnika

Iff S, Craig JC, Turner R, et al. Reduced estimated GFR and cancer mortality. Am J Kidney Dis 2014; 63:23.
Na SY, Sung JY, Chang JH, et al. Chronic kidney disease in cancer patients: an independent predictor of cancer-specific mortality. Am J Nephrol 2011; 33:121.
Königsbrügge O, Lötsch F, Zielinski C, et al. Chronic kidney disease in patients with cancer and its association with occurrence of venous thromboembolism and mortality. Thromb Res 2014; 134:44.

Smrtnost u onkoloških bolesnika s KBB

- Onkološki bolesnici s KBB mogu imati povećan mortalitet u odnosu na one bez KBB
- Rizik je varijabilan (ovisno o literaturnim podacima)
- U nekim studijama pak bez razlike u smrtnosti u onkoloških bolesnika s i bez KBB

Iff S, Craig JC, Turner R, et al. Reduced estimated GFR and cancer mortality. Am J Kidney Dis 2014; 63:23.
Na SY, Sung JY, Chang JH, et al. Chronic kidney disease in cancer patients: an independent predictor of cancer-specific mortality. Am J Nephrol 2011; 33:121.
Königsbrügge O, Lötsch F, Zielinski C, et al. Chronic kidney disease in patients with cancer and its association with occurrence of venous thromboembolism and mortality. Thromb Res 2014; 134:44.
Yang Y, Li HY, Zhou Q, et al. Renal Function and All-Cause Mortality Risk Among Cancer Patients. Medicine (Baltimore) 2016; 95:e3728.

KBB – rizični faktor za maligne bolesti?

- Retrospektivna studija; SAD; 2014; 1,190,538 odraslih pacijenata; period 2000-2008; negativna anamneza za maligne bolesti;
- Niža eGFR – čimbenik povećanog rizika za karcinom bubrega i karcinome urotela (HR 2.3, 95% confidence interval [CI] 1.8-2.9 za eGFR of <30 mL/min/1.73 m) no ne i za druge tumorske bolesti
- Bolesnici s terminalnom fazom KBB koji se liječe dijalizom; povećan rizik carcinoma bubrega – stečene ciste

Lowrance WT, Ordoñez J, Udaltsova N, et al. CKD and the risk of incident cancer. J Am Soc Nephrol 2014; 25:2327.

Stewart JH, Buccianti G, Agodoa L, et al. Cancers of the kidney and urinary tract in patients on dialysis for end-stage renal disease: analysis of data from the United States, Europe, and Australia and New Zealand. J Am Soc Nephrol 2003; 14:197.

Maisonneuve P, Agodoa L, Gellert R, et al. Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. Lancet 1999; 354:93.

Zaključno

- AKI i KBB česti u onkoloških bolesnika
- dob vs komorbiditeti
- definicija
- mortalitet
- procjena bubrežne funkcije

Hvala na pažnji!