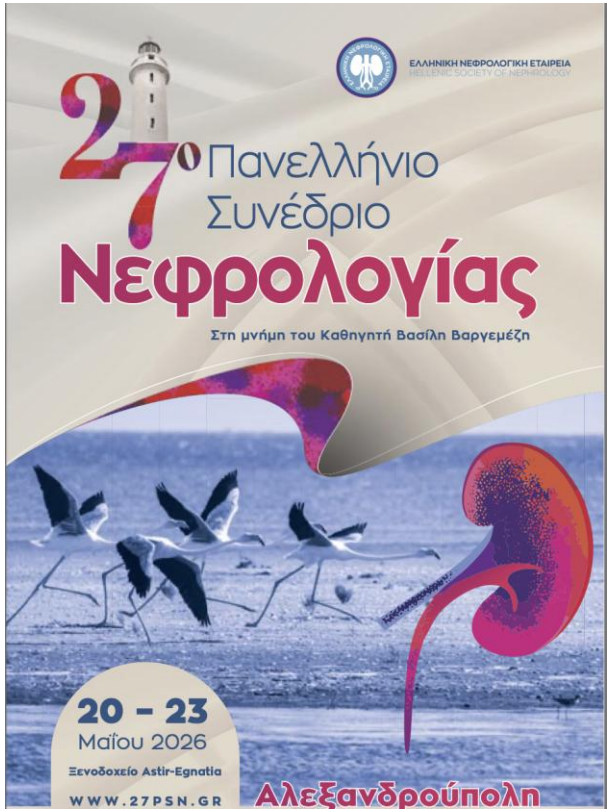
Πανεπιστημιακο
Γενικο Νοσοκομειο Ιωαννινων



Acute Kidney Disease:

Does This Entity Exist?

Eleni Stamellou, MD PhD
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The Problem: A Critical Diagnostic Gap

AKI

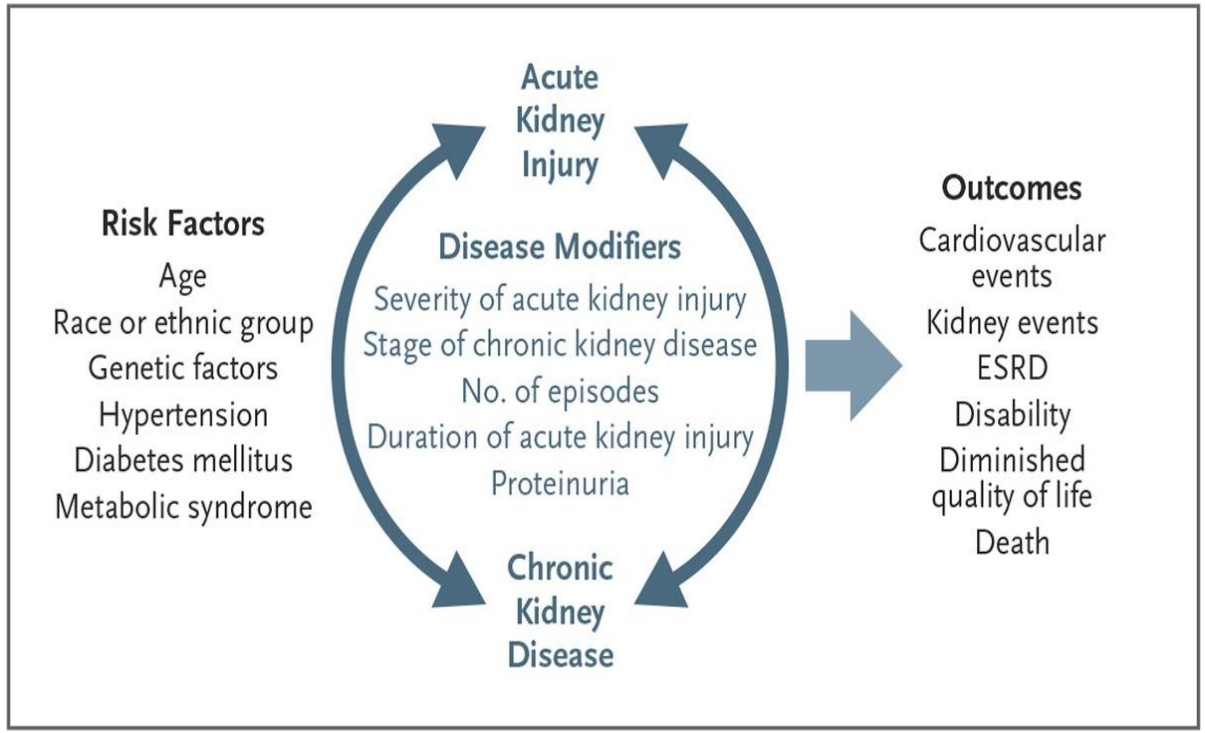
< 7 days

Well-defined

KDIGO criteria
(SCr, UO)

AKI and CKD: interconnected syndromes

- AKI and CKD share common risk factors
- CKD is an important risk factor for AKI
- AKI contributes to progression of CKD
- CKD impairs recovery after AKI



Chawla LS et al. N Engl J Med 2014;371:58-66.

The Problem: A Critical Diagnostic Gap

AKI

< 7 days

Well-defined

KDIGO criteria
(SCr, UO)

CKD

> 90 days

Well-defined

eGFR <60 or
albuminuria >3 months

AKD fills this gap — but is this enough to make it a real, clinically meaningful entity?

Acute Kidney Disease

Why introduce AKD?

→ Many patients fall between AKI and CKD definitions — they need a home

→ Pathophysiologic processes persist and are ongoing after the initial insult

→ The 7–90 day window is critical: repair vs. fibrosis pathways compete

→ A clear taxonomy enables research, guidelines and clinical management

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Chawla LS, et al. Acute kidney disease and renal recovery: consensus report of the ADQI 16 Workgroup. Nat Rev Nephrol. 2017;13(4):241-257.

Acute Kidney Disease Definition

2012 → **2017**

2012 KDIGO AKI Workgroup

Any acute condition that affects kidney function:

- AKI
- GFR < 60 ml/min/1.73m^2 for < 3m
- ↓GFR by ≥35%
- ↑ SCr of > 50% for < 3 m
- any kidney damage < 3 m

ADQI 16 Workgroup Definition

AKD is defined as AKI stage ≥1, present **≥7 days** after an AKI initiating event.

AKD persisting beyond **90 days** = CKD.

An AKI initiating event can usually be identified but is *not required* to diagnose AKD.

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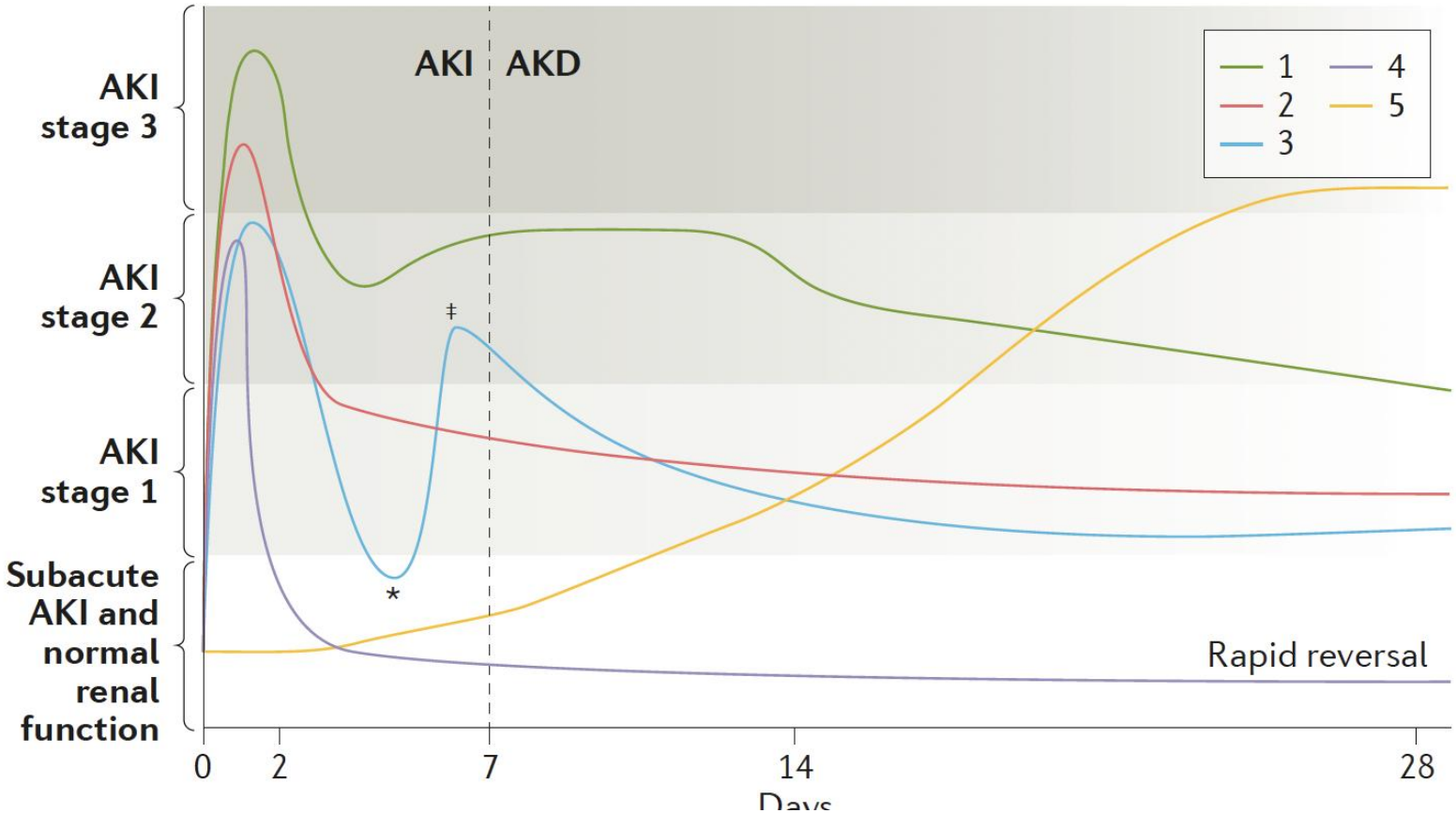
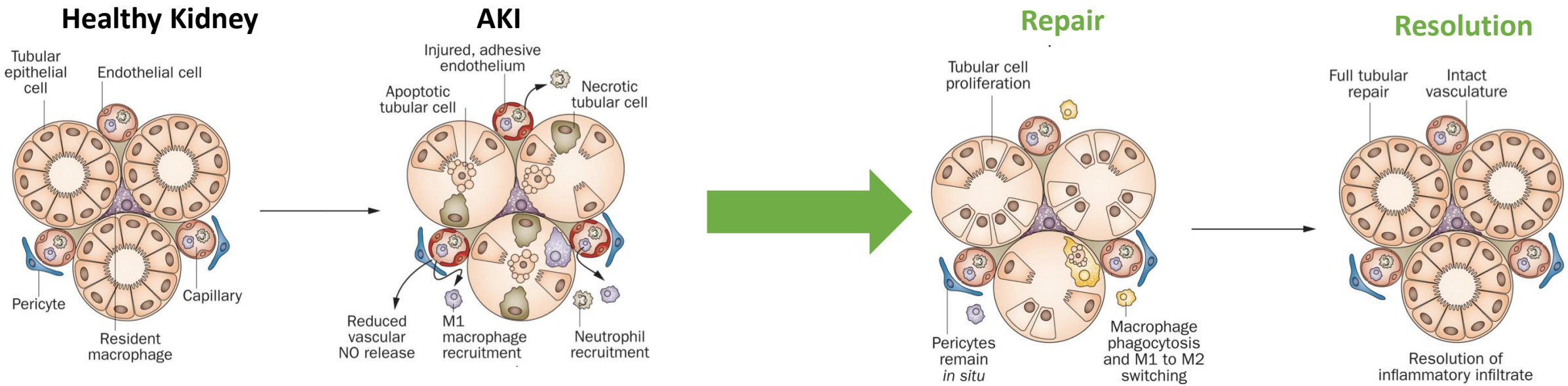
AKD Trajectories

No CKD No AKI	AKI	AKD 7–90 days	CKD > 90 days



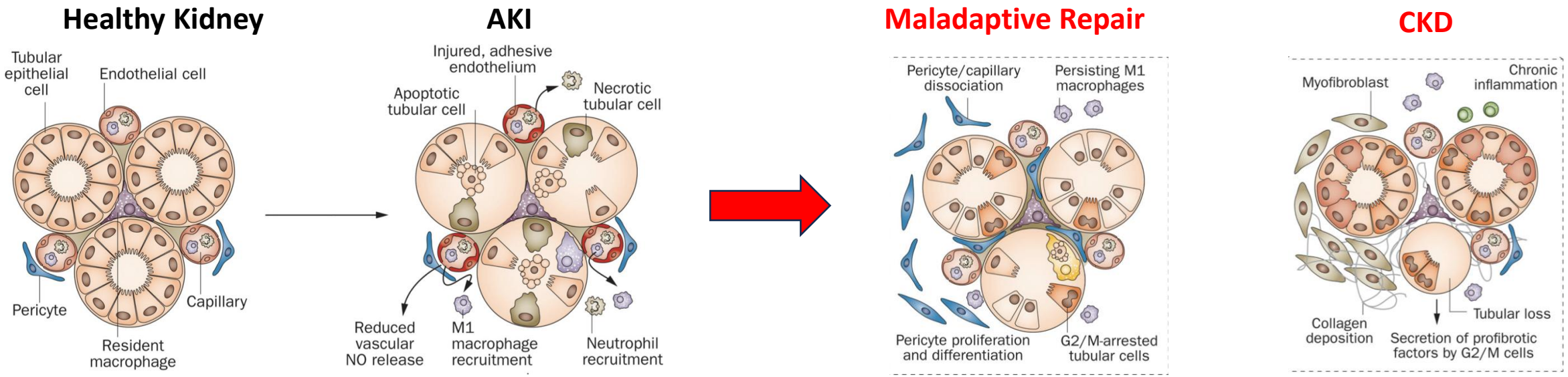
Modified from: Chawla LS, et al. Nat Rev Nephrol. 2017;13:241-257. | Lameire NH, et al. Kidney Int. 2021;100:516-526.

AKI-AKD-CKD: Pathophysiological Cascade

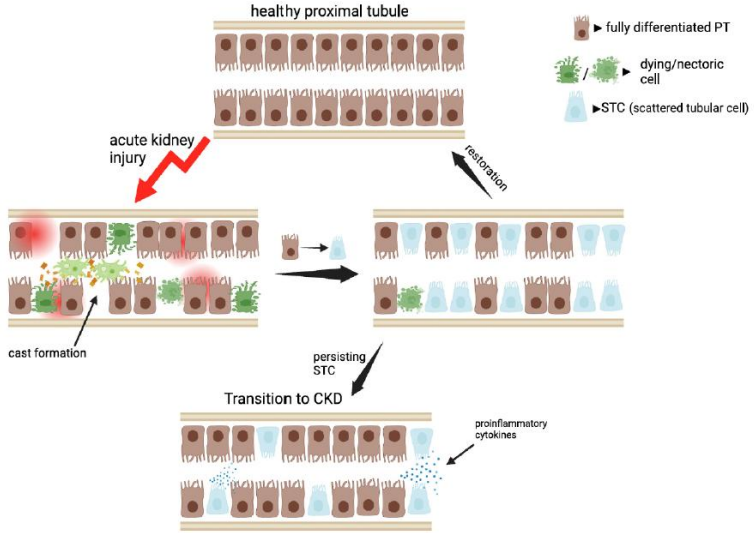


Natue Rev Nephrol. 2015 May;11(5):264-76.

AKI-AKD-CKD: Pathophysiological Cascade



1. ***Νέκρωση κυττάρων, απώλεια νεφρώνων και ίνωση***
2. ***Προσαρμογή, Αναγέννηση και Δυσαρμονία Κυττάρων***



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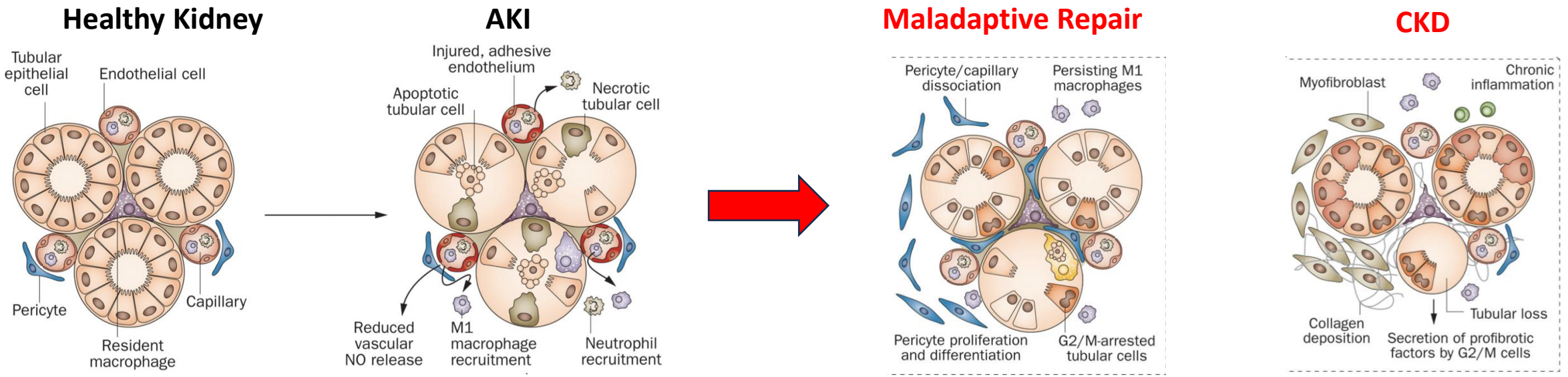
AKI-AKD-CKD: Pathophysiological Cascade



1. *Νέκρωση κυττάρων, απώλεια νεφρώνων και ίνωση*
2. *Προσαρμογή, Αναγέννηση και Δυσαρμονία Κυττάρων*
3. *Αγγειακή απορρύθμιση και ιστική υποξία*
4. *Ανοσοκύτταρα και φλεγμονώδη απόκριση στην ΟΝΒ*

Μετάβαση από ΟΝΒ σε ΧΝΝ

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Natue Rev Nephrol. 2015 May;11(5):264-76.

Η AKD αντιπροσωπεύει το χρονικό παράθυρο όπου η πορεία της νόσου παραμένει ακόμη αναστρέψιμη, αλλά είναι εξίσου πιθανό να στραφεί προς χρόνια ίνωση.

Functional Recovery Does Not Equal Structural Recovery

SCr / eGFR normalization after AKI ≠ complete kidney tissue repair

What the labs show:

- ✓ Serum creatinine returns to baseline
- ✓ eGFR appears 'normal'
- ✓ Patient is declared 'AKI resolved'
- ✓ Often discharged — no nephrology follow-up

Functional Recovery Does Not Equal Structural Recovery

Current kidney function parameters overestimate kidney tissue repair in reversible experimental kidney disease

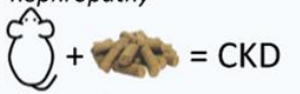
kidney INTERNATIONAL

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Methods:

Experimental models:

a) 2,8-dihydroxyadenine nephropathy



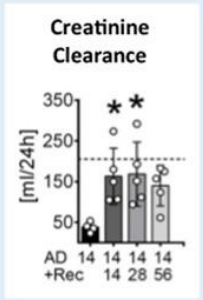
b) reversible unilateral ureteral obstruction

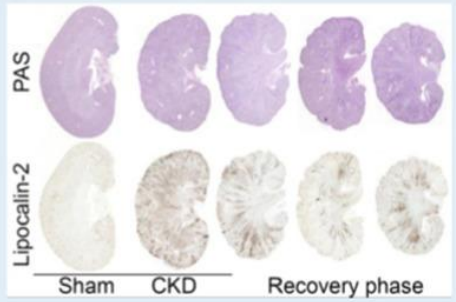
- *reversibility & regeneration*
- *therapeutic high fluid intake*

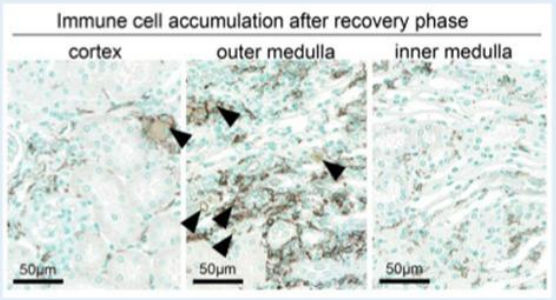
Results:

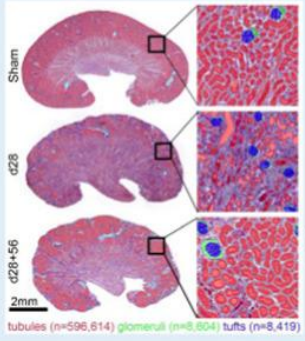
During recovery from CKD:

- kidney function improves
- tissue injury and fibrosis persist, particularly in the medulla

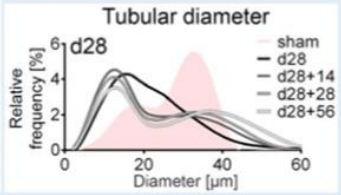






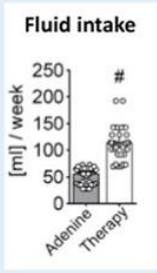


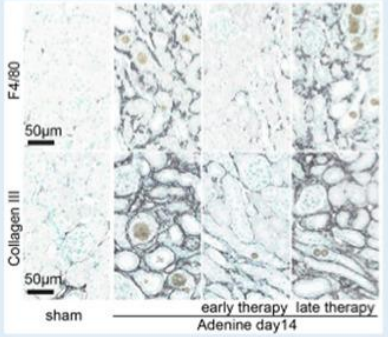
AI-augmented histological analysis reveals tubular fate: regeneration, dilation, hypertrophy or atrophy



Therapeutical increase of drinking volume:

- only effective in early but not advanced CKD
- effects are poorly reflected by kidney function





Klinkhammer et al., 2022

CONCLUSION: *Recovery after crystal- or obstruction-induced CKD is characterized by ongoing tissue injury, fibrosis, and nephron loss, which is not reflected by standard kidney function parameters.*

- ✓ Microvascular rarefaction
- ✓ Pro-fibrotic gene expression
- ✓ Nephron mass is reduced

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Biomarkers in AKD

- Il-18
- NGAL
- CyS
- KIM-1

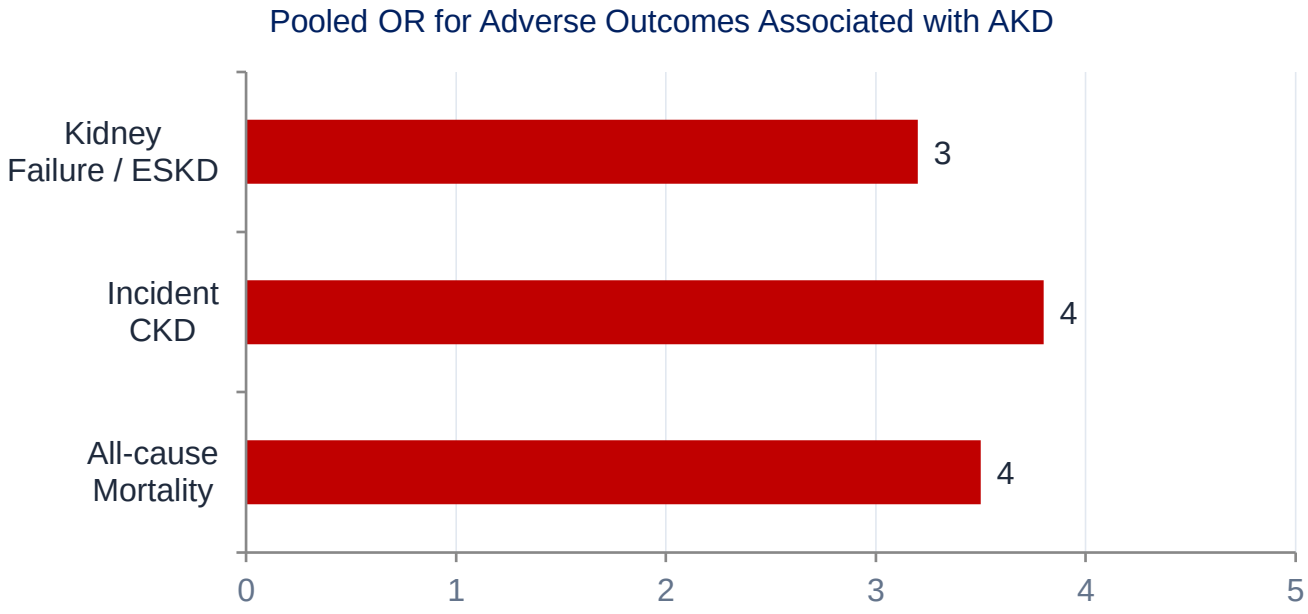
AKD Is Highly Prevalent

59
Studies included

~6M
Participants

11.1%
Pooled incidence
(KDIGO criteria)

26.6%
Pooled incidence
(ADQI criteria)



AKD triples mortality risk

Regardless of which definition is used, patients with AKD have 3–4× higher odds of:

- Death
- Incident CKD
- Kidney failure / ESKD

This is not a semantic label.
This is a prognostic entity.

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Yang C, et al. Incidence and Adverse Outcomes of AKD: Systematic Review & Meta-Analysis (~6M participants). Am J Kidney Dis. 2025. | Su CC, et al. eClinicalMedicine. 2022;55:101760.

AKD Is Highly Prevalent

21

Studies included
1,114,012 patients

26.11%

Hospital-acquired AKD
with prior AKI

4.60%

Community-acquired AKD
incidence rate

2.11%

Hospital-acquired AKD
without prior AKI

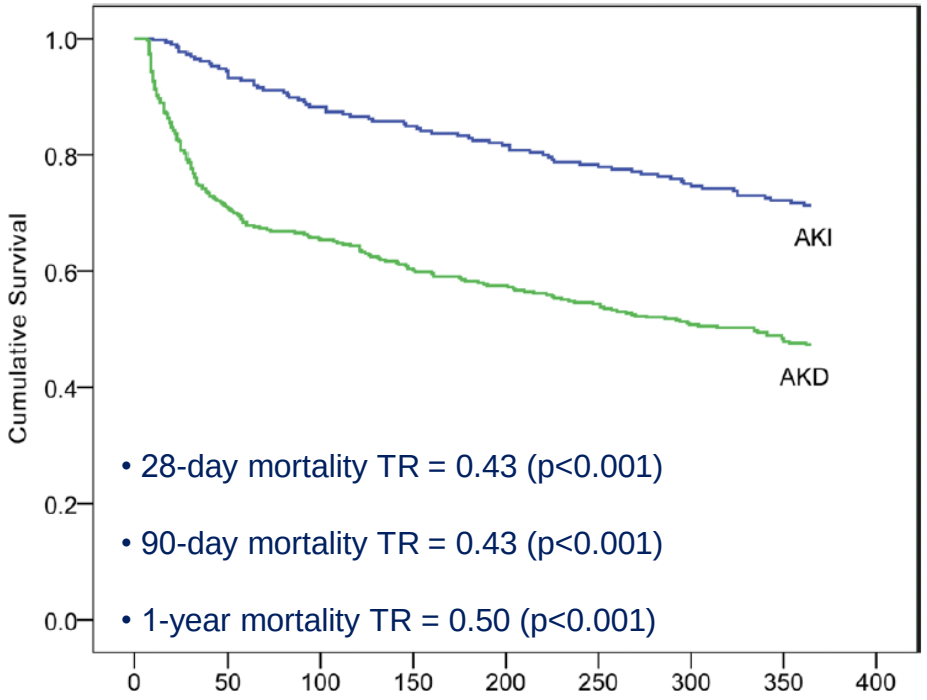
Clinical Outcomes: AKD vs. No Kidney Disease (NKD)

All-cause mortality: **AKD 26.54% vs. NKD 7.78% (OR 3.62; 95% CI 2.64-4.95)**
Progression to ESKD: **AKD 1.3% vs. NKD 0.14% (OR 6.58; 95% CI 3.75-11.55)**
Incident/progressive CKD: **AKD 37.2% vs. NKD 7.45% (OR 4.22; 95% CI 2.79-6.39)**
AKD without prior AKI: **Still 3x higher mortality (OR 3.00) and ESKD risk (OR 4.96) vs. NKD**

Su CC, et al. Outcomes associated with acute kidney disease: a systematic review and meta-analysis. eClinicalMedicine. 2023;55:101760.

AKD is highly prevalent in high-risk populations

Elderly patients: 61% developed AKD



Critically ill patients

- Study of 1231 AKI patients with sepsis **46.9%** of patients **developed AKD**
- Single-center retrospective analysis of 256 patients with septic AKI, **53.9% developed AKD**

Elderly patients with AKD face profoundly worse outcomes across all time horizons —> represent the cohort most in need of structured AKD follow-up pathways.

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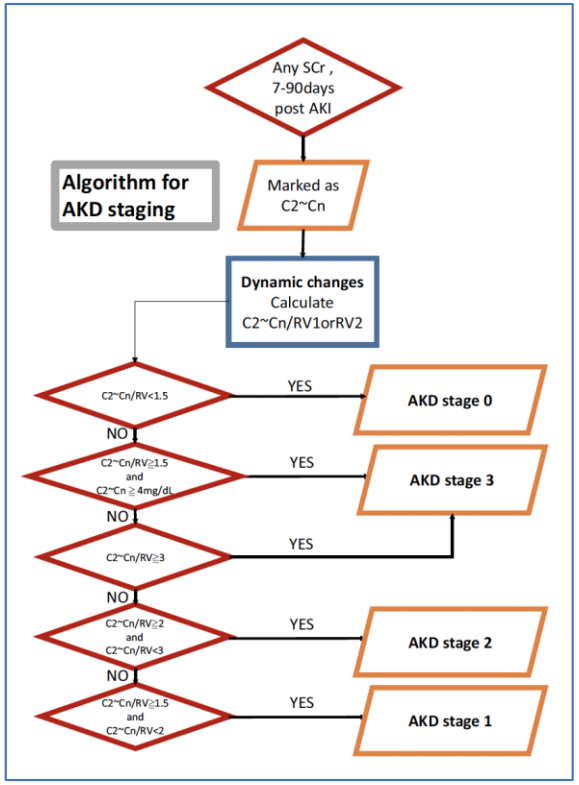
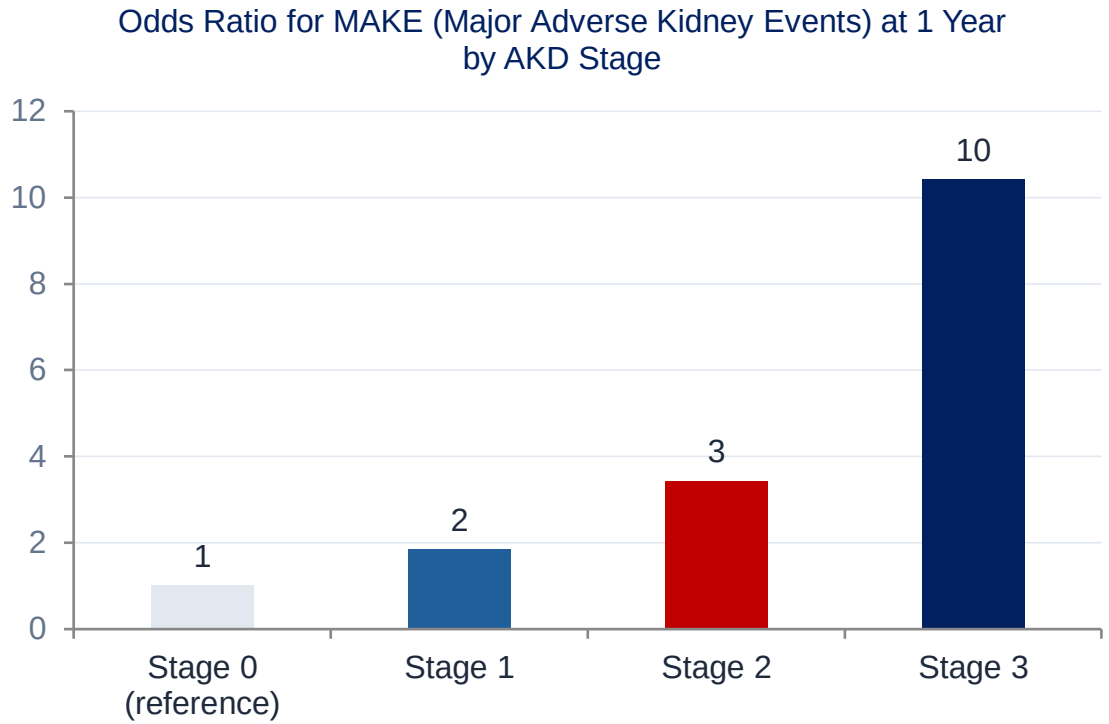
Li Q, et al. Short- and long-term outcomes of elderly patients with AKI to AKD. J Intensive Care. 2026;14:41. (1,395 patients ≥75 yrs, Chinese PLA General Hospital)

AKD Staging Has Independent Prognostic Value





MAKE = Major Adverse Kidney Events

- eGFR decline >35% from baseline
- Initiation of dialysis
- In-hospital mortality

Stage 3 AKD

OR **10.41**

for MAKE at 1 year

Regardless of baseline eGFR, staging identifies high-risk patients.

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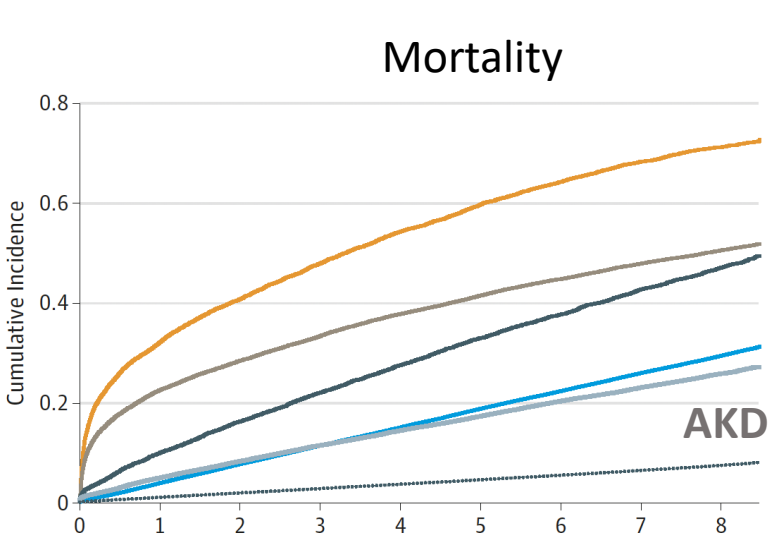
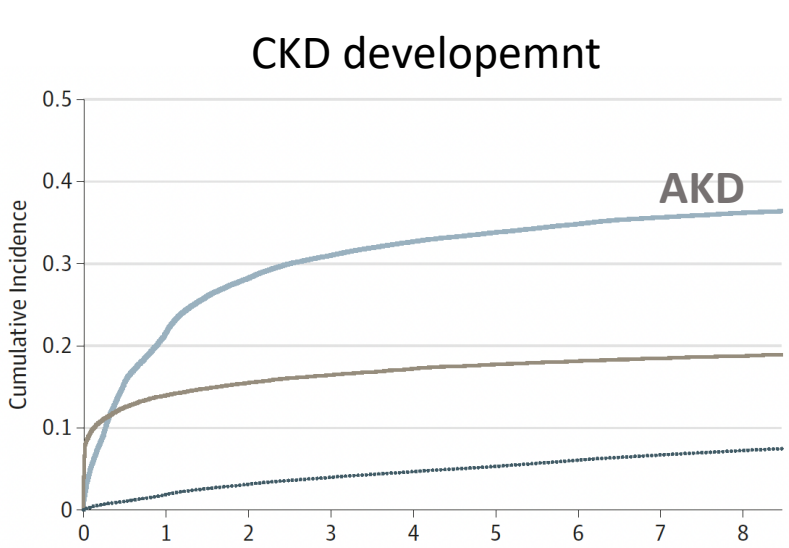
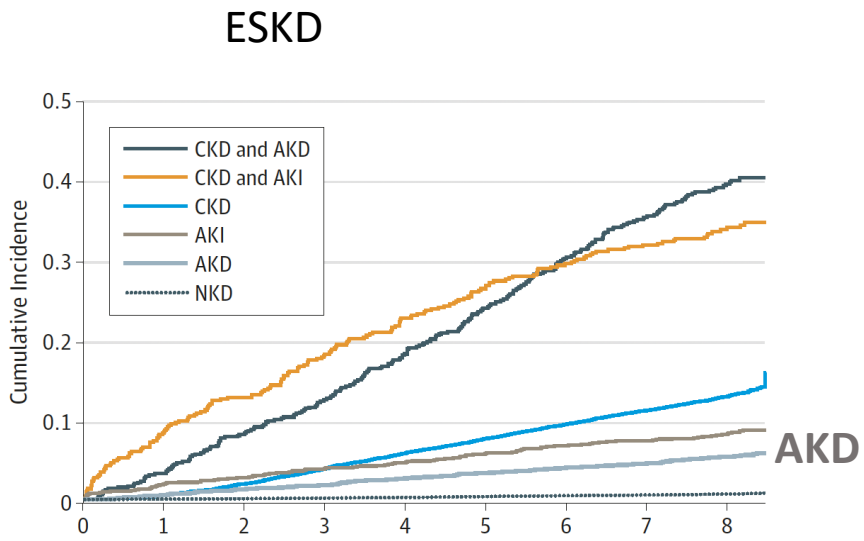
Chen YW, et al. Severe acute kidney disease is associated with worse kidney outcome. Sci Rep. 2022;12:5785. (n=4,741 AKI patients)

AKD Without AKI Is ALSO a Distinct Clinical Entity

- 1.1 M residents (Alberta, Canada)
- **10%** developed **AKD** without prior AKI







The patients who never met AKI criteria but had subacute kidney function decline — the **AKD-without-AKI group — still faced significantly increased risk of CKD progression, ESKD, and death.**

AKD can occur DE NOVO — without any preceding AKI episode

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James MT, et al. Incidence and Prognosis of Acute Kidney Diseases and Disorders. JAMA Intern Med. 2019;179(11):1536-1544. (Universal health care system, 1.1 million residents)

Risk Factors for AKD Development after AKI

Patient-related factors

- ✓ **Older age** (OR 1.05-1.758 per year)
- ✓ **Female sex** (male sex protective: OR 0.45-0.78)
- ✓ **Pre-existing CKD** (up to 6x higher risk; OR 1.46-1.54)
- ✓ **Hypertension** (OR 3.05; 95% CI 2.66-3.50)
- ✓ **Chronic heart failure** (OR 4.83; 95% CI 4.09-5.69)
- ✓ **Diabetes mellitus** (OR 1.58; 95% CI 1.39-1.80)
- ✓ **Malignancy** (OR 3.10; 95% CI 2.49-3.87)
- ✓ **Liver disease** (OR 1.43; 95% CI 1.27-1.61)

AKI-related & iatrogenic factors

- ✓ **AKI** stage 3 ↑ AKD risk up to 34x (OR 34.1)
- ✓ **Persistent AKI (>48 h)** higher risk than transient AKI (HR 6.26)
- ✓ **Nephrotoxic medications** >3x risk for AKD stage 3 (OR 3.13)
- ✓ **Surgical setting** cardiac/vascular: AKD in 12-74% of AKI patients
- ✓ **Critical illness / Sepsis** AKD in 47-54% of septic AKI
- ✓ **Hypoalbuminemia / Anemia** albumin <3.5 g/dl (OR 1.48); Hb <10 g/dl (OR 1.46)
- ✓ **Biomarkers** elevated IL-18, NGAL, cystatin C predictive of AKD

Gameiro J, et al. The burden of acute kidney disease: an epidemiological review and importance of follow-up care. Clin Kidney J. 2025;18(6):sfaf169.

KDIGO Guideline: Mandatory Post-AKI Evaluation

Recommendation 2.3.4 (Not Graded)

"Evaluate patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD. If patients have CKD, manage these patients as detailed in the KDIGO CKD Guideline."

KAMPS Framework for AKD Transition of Care

K	A	M	P	S
Kidney function check	**Advocacy**	**Medications**	**Pressure**	**Sick-day rules**
Monitor SCr, eGFR, urinalysis	Ensure nephrology referral is made	Review, adjust, avoid nephrotoxins	BP target <130/80 mmHg	Patient education and self-monitoring

KDIGO AKI Clinical Practice Guideline, Recommendation 2.3.4. | Goldstein SL, et al. CJASN. 2013;8:476-483.

Early initiation or reinitiation of RAAS inhibitors reduces mortality after AKI

Όσο νωρίτερα συνταγοραφούνται οι RAASi μετά την έξοδο από το νοσοκομείο , τόσο χαμηλότερο ήταν το ποσοστό θνητότητας τα επόμενα 1-10 χρόνια.

- ✓ 54.736 ασθενείς με διαβητική νεφροπάθεια
- ✓ **Συνολική θνησιμότητα**

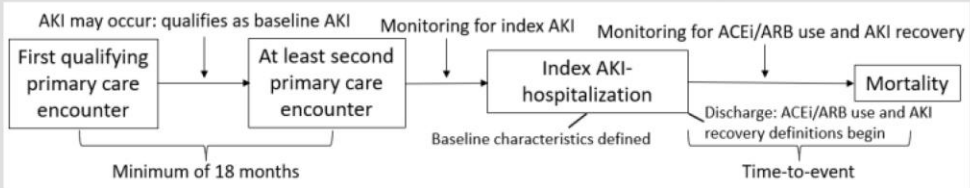
30% μείωση κινδύνου θνησιμότητας!!

RAAS Blockade after Acute Kidney Injury with or without Recovery among Veterans with Diabetic Kidney Disease

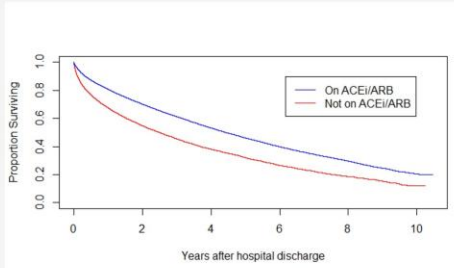
JASN JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

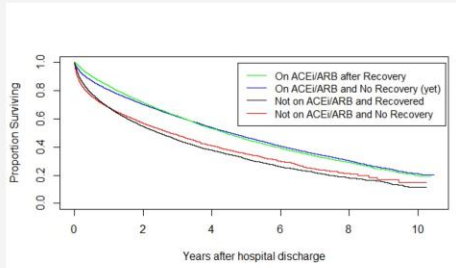
Methods

Retrospective cohort of 54,735 Veterans with diabetic kidney disease assessed for time-varying post-AKI ACEi/ARB use and time-varying AKI-recovery. Study outcome was all-cause mortality.



Outcome





Conclusion

This study demonstrated lower mortality associated with ACEi/ARB use in Veterans with diabetes mellitus, proteinuria, and AKI regardless of AKI recovery. Results favored earlier ACEi/ARB initiation or resumption, though results continued to favor ACEi/ARB initiation later after AKI.

10.1681/ASN.0000000000000196

J Am Soc Nephrol. 2023Oct1;34(10):1721-1732.

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Conclusions

1. YES — AKD is a real entity. It fills a critical, clinically validated gap between AKI (<7 days) and CKD (>90 days).
2. AKD is highly prevalent: pooled incidence 11–27% across ~6 million patients — a global health burden.
3. AKD carries severe prognostic implications: 3–4× higher odds of death, CKD progression, and ESKD.
4. Structured nephrology follow-up in the AKD period improves survival — KDIGO mandates it for good reason.