



MÁSTER EN HEPATOLOGÍA

UAM
Universidad Autónoma
de Madrid

 Universidad
de Alcalá

Asignatura: Cirrosis III

“Insuficiencia renal en la cirrosis. Insuficiencia renal en la cirrosis por MAFLD”

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Disclosure of interests

PERE GINÈS

I disclose the following financial relationship(s) with a commercial interest:

Mallinckrodt, Novartis, Sequana Medical, Gilead,
Grifols, Martin Pharmaceuticals, Intercept, Echosens

OUTLINE

- Definition and prevalence of AKI in cirrhosis
- Staging and main etiologies of AKI
- Kidney biomarkers and AKI in cirrhosis
- Algorithm for diagnosis and management of AKI in cirrhosis
- CKD. Role of MAFLD. Transition from AKI to CKD

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ACUTE KIDNEY INJURY IN CIRRHOSIS

International Club of Ascites (ICA-AKI) definition

Increase in sCr ≥ 0.3 mg/dL (≥ 26.5 $\mu\text{mol/L}$) within 48 h; or increase of $>50\%$ from baseline which is known, or presumed, to have occurred within the prior 7 days. Values up to the previous 3 months can be used as baseline

Examples:

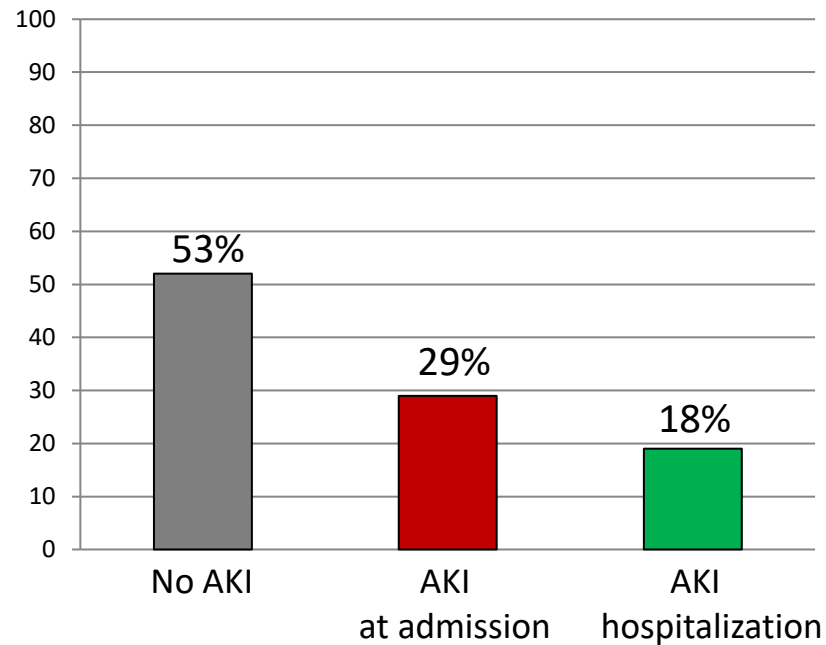
Baseline	AKI	Diagnosis
0.7 mg/dL	2.6 mg/dL	AKI
0.9 mg/dL	1.2 mg/dL	AKI
1.8 mg/dL	3.2 mg/dL	AKI on CKD
-----	2.5 mg/dL	AKI or CKD?

Angeli P et al , J Hepatol 2015

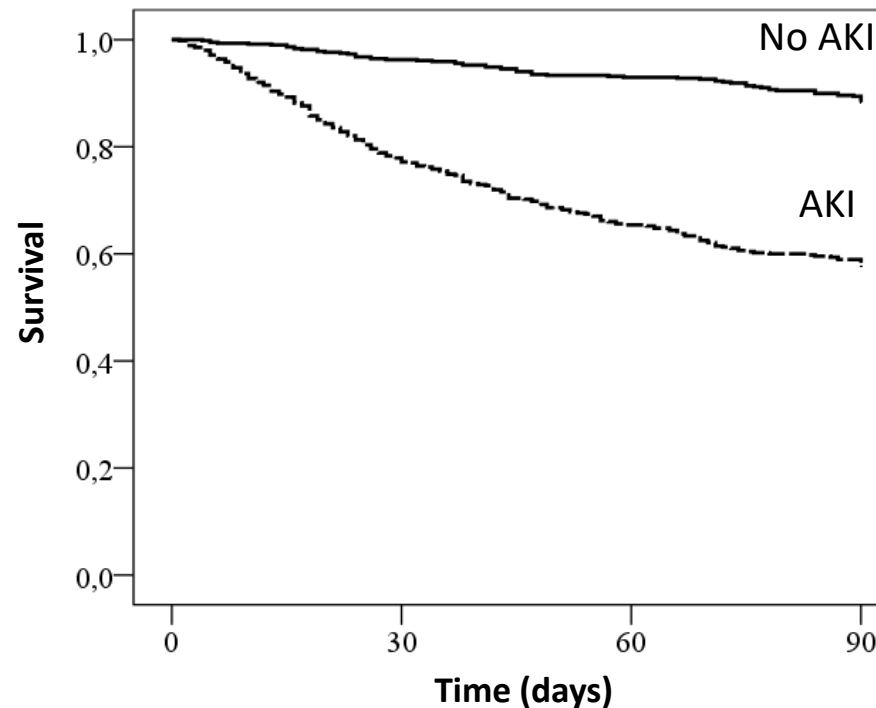
PREVALENCE OF AKI AND PROGNOSIS

Hospitalized patients with decompensated cirrhosis (n=1155)

Prevalence

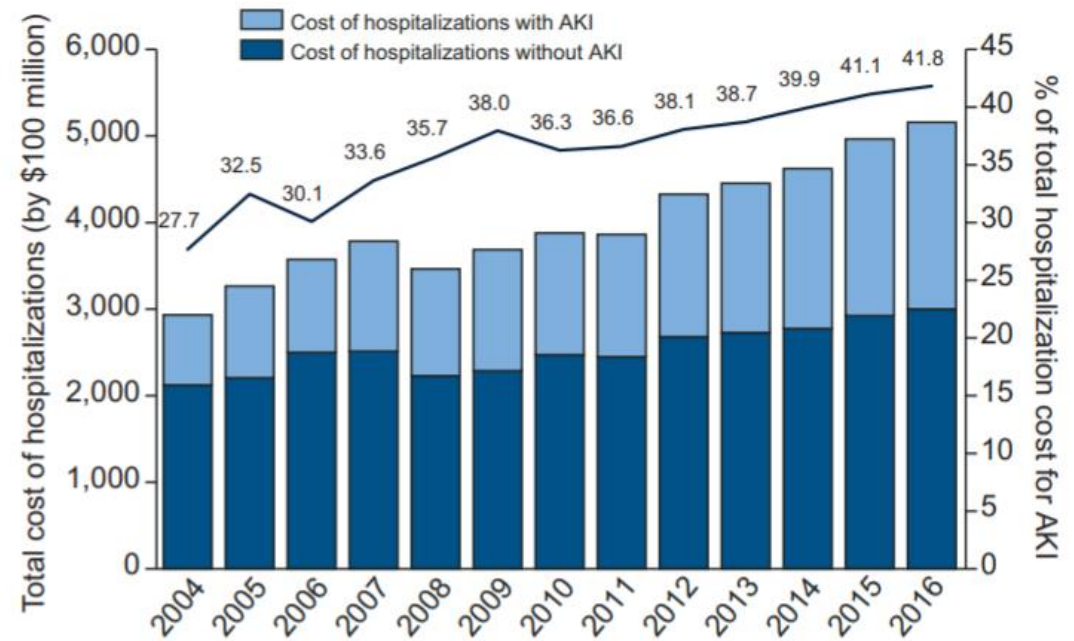
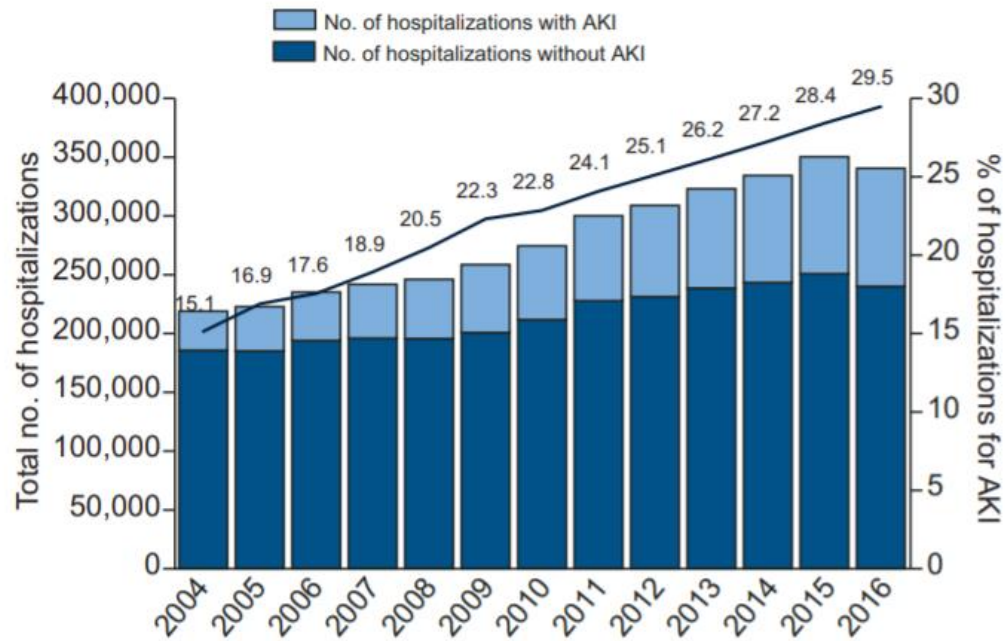


Survival



Huelin P. et al, Clin Gastroenterol Hepatol 2017

BURDEN OF AKI IN CIRRHOSIS IN USA



Desai et al. JHepatol.2020

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ACUTE KIDNEY INJURY IN CIRRHOSIS

International Club of Ascites (ICA-AKI) definition

Staging of AKI

Stage AKI	CRITERIA
Stage 1 68%	increase in sCr ≥ 0.3 mg/dL (26.5 mmol/L) or an increase in sCr ≥ 1.5 -fold to twofold from baseline Stage 1A sCr at diagnosis: < 1.5 mg/dL 20% Stage 1B sCr at diagnosis: ≥ 1.5 mg/dL 48%
Stage 2 19%	increase in sCr >two to threefold from baseline
Stage 3 13%	increase of sCr >threefold from baseline or sCr ≥ 4.0 mg/dL (353.6 mmol/L) with an acute increase ≥ 0.3 mg/dL (26.5 mmol/L) or initiation of renal replacement therapy

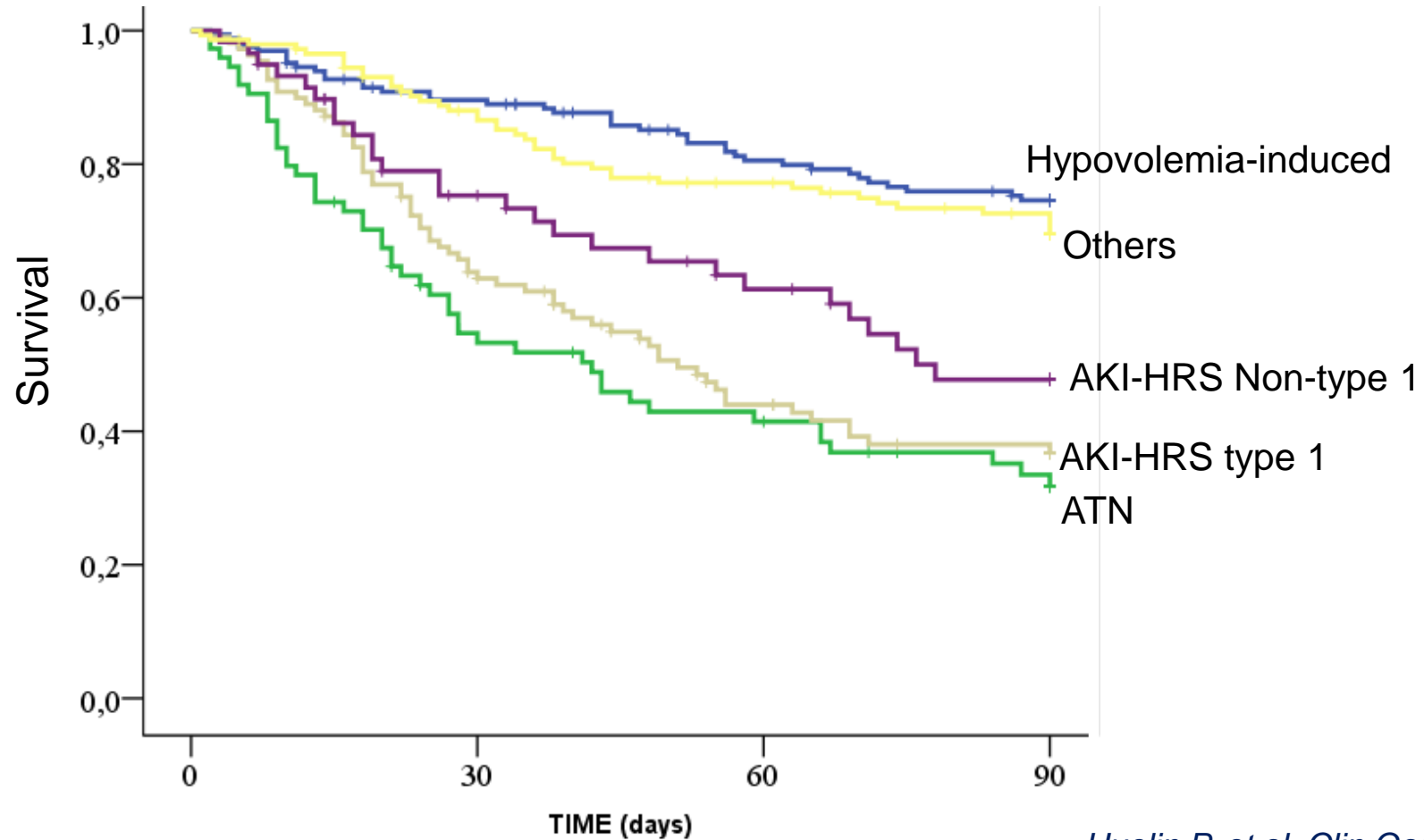
Angeli P et al , J Hepatol 2015

MAIN ETIOLOGIES OF AKI IN CIRRHOSIS

- **HYPOVOLEMIA-INDUCED** (*diuretics, GI bleeding, diarrhea*).
- **HEPATORENAL SYNDROME**
- **ACUTE TUBULAR NECROSIS** (*shock, nephrotoxic drugs, other*).
- **NON-STEROIDAL ANTIINFLAMMATORY DRUGS** (*NSAIDs*)
- **GLOMERULONEPHRITIS**
- **MISCELLANEOUS/UNKNOWN**

PROGNOSIS OF AKI IN CIRRHOSIS

Relevance of the etiology of AKI



Huelin P. et al, Clin Gastroenterol Hepatol 2017

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KIDNEY BIOMARKERS IN CIRRHOSIS

Potential usefulness

Help in differential diagnosis of AKI (ATN vs HRS)

Provide information on kidney outcomes

Provide prognostic information

Provide information on reversibility after transplantation

DIFFERENTIAL DIAGNOSIS OF AKI IN CIRRHOSIS

Urine NGAL for diagnosis of ATN vs other types of AKI

Author (year)	Patients included			Day of urine collection	AUROC ATN vs other	Cut-off value	Sn/Sp (%)*
	AKI (n)	HRS (n)	ATN (n)				
Fagundes (2012)	84	33	11	AKI diagnosis	NA	194 µg/g	91/82
Verna (2012)	52	20	15	AKI diagnosis	0.86	110 ng/mL	88/85
Belcher (2014)	76	16	39	median 2 days after AKI diagnosis	0.78	365 ng/mL	NA
Ariza (2015)	39	12	15	AKI diagnosis ±1 day	0.95	294 µg/g	92/89
Huelin (2019)	320	93	39	AKI diagnosis and day 3**	0.87	220 µg/g	88/85

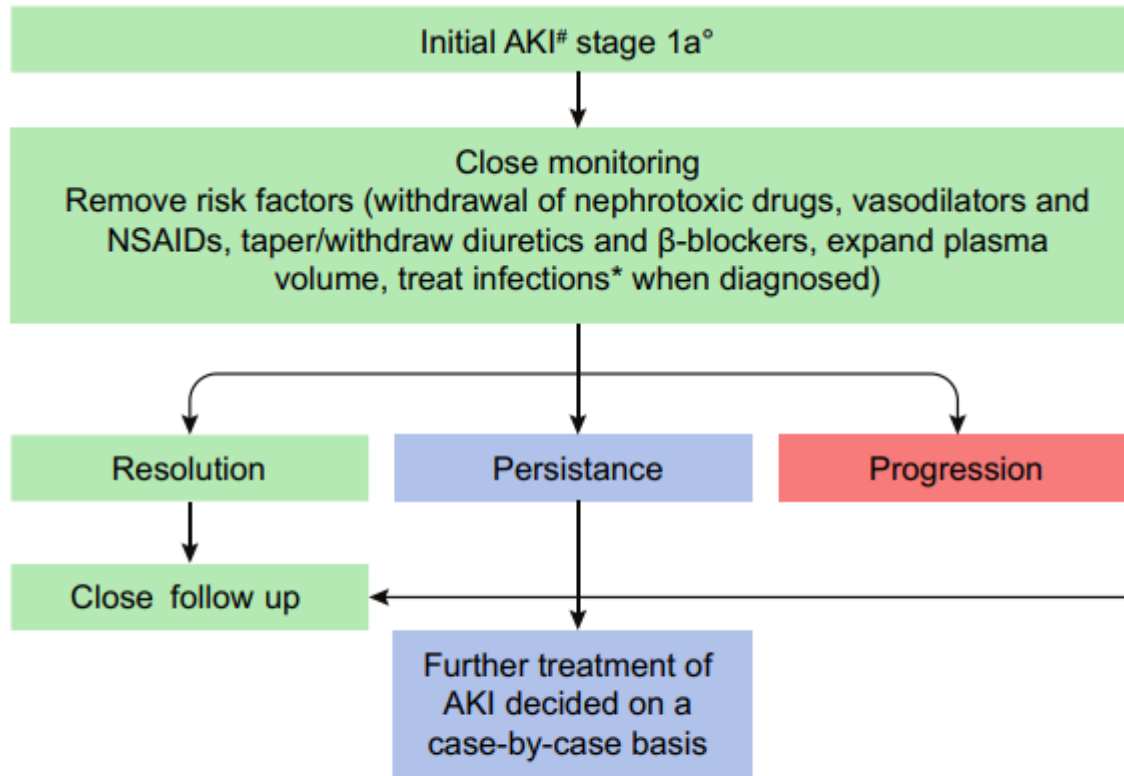
*Sensitivity/Specificity

** Urine was collected at diagnosis of AKI and at day 3. Values shown in the table are those of day 3.

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EASL GUIDELINES ALGORITHM FOR AKI DIAGNOSIS AND MANAGEMENT



*AKI at the first fulfilling of KDIGO criteria

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CKD IN CIRRHOSIS

Definition: Estimated GFR < 60 ML/min for more than 3 months

Two main types of CKD in cirrhosis

- Functional: HRS-CKD (“type-2 HRS”)
- Structural: MAFLD-associated (combination of factors)

Transition from AKI to CKD

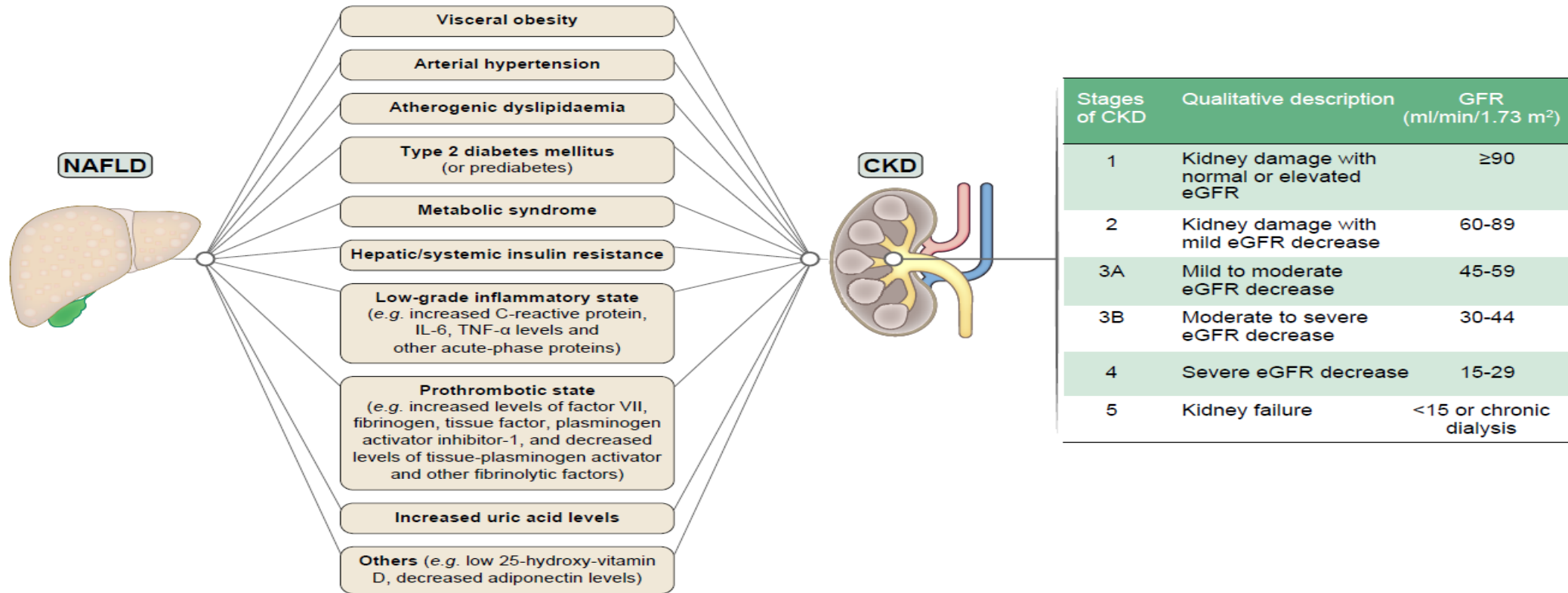
Glomerulonephritis (i.e IgGA)

CKD IN CIRRHOSIS

Clinical consequences

- Poor response to diuretics; refractory ascites common
- Hyponatremia, HE, and AKI frequent with diuretic therapy
- Increased hospitalizations
- Increased risk of complications of cirrhosis (AKI, HE, infections)
- Poor outcome before transplantation
- Worse outcome after transplantation vs patients without CKD

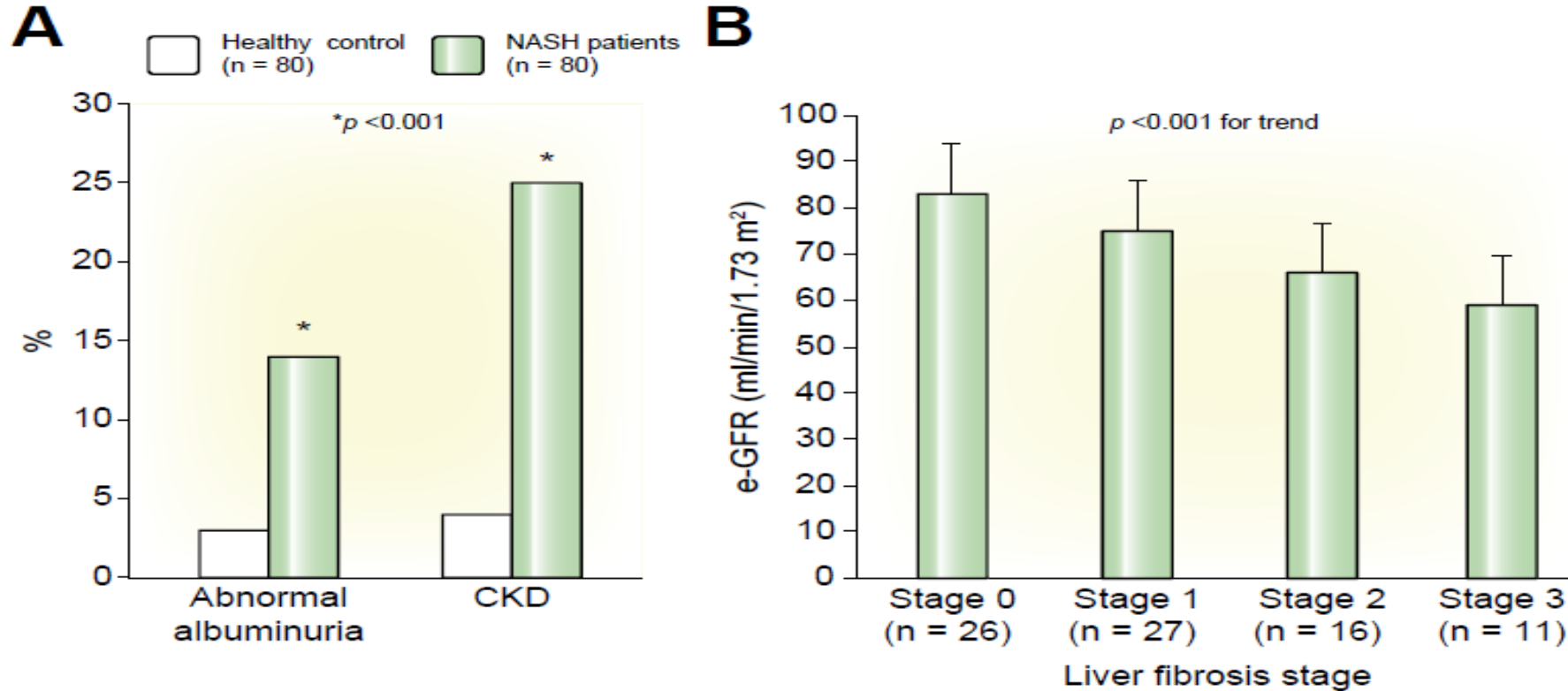
CKD AND MAFLD



Byrne. JHepatol.2020

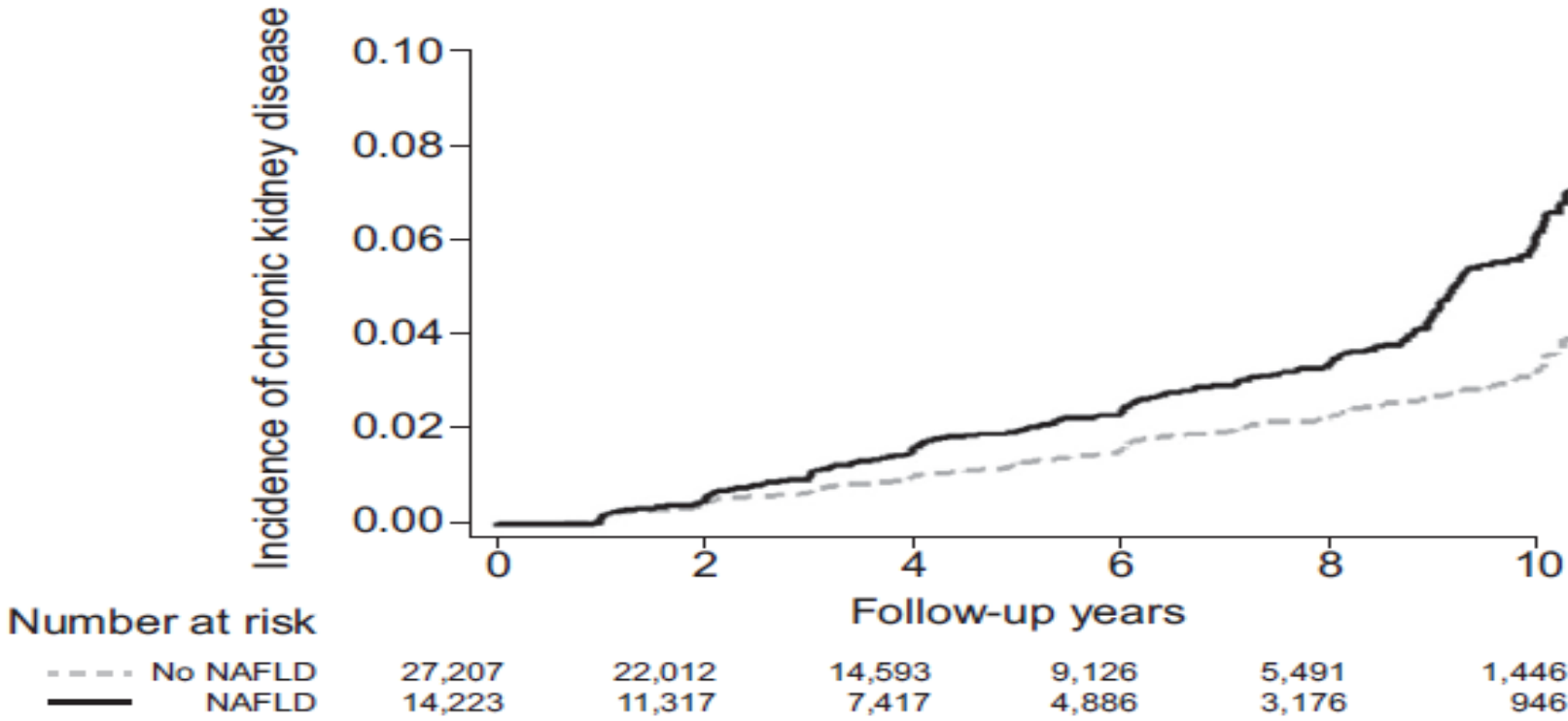
CKD AND MAFLD

Relationship with fibrosis stage



Byrne. JHepatol.2020

CKD AND MAFLD



Hyun Sinn. JHepatol.2017

TAKE-HOME MESSAGES (1)

- The diagnostic criteria of AKI are helpful for early detection of impairment in kidney function
- Categorization of patients with AKI stage 1 into 1A and 1B identifies subgroups with very different kidney and patient outcomes
- Etiology of AKI is an important determinant of prognosis, mortality being higher for hepatorenal syndrome and acute tubular necrosis vs hypovolemia-induced AKI
- Urine NGAL is useful in the differential diagnosis between ATN vs other etiologies of AKI in cirrhosis and also for outcome prediction

TAKE-HOME MESSAGES (2)

- CKD is common in patients with cirrhosis and is defined by a persistent reduction in eGFR (<60 mL/min) for more than 3 months
- Development of CKD is associated with an increased risk of complications, particularly AKI, refractory ascites, and bacterial infections, and increased 3-month readmission rate
- CKD is common in patients with MAFLD and its frequency increases in parallel with progression of liver fibrosis
- CKD identifies a high-risk group of patients with cirrhosis



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