Acute kidney injury in patients with cirrhosis

P. Angeli, Dept. of Medicine,
Unit of Internal Medicine and Hepatology (UIMH),
University of Padova (Italy)
pangeli@unipd.it

XXIV Congreso de la Asociación Latinoamericana para el Estudio del Hígado (ALEH)
Santiago (Chile) September 28- October 1 2016
Definition of renal failure in cirrhosis

- The traditional diagnostic criteria of renal failure in cirrhosis were proposed more 20 years ago and have been improved in subsequent years.

- It was based on the presence of a serum creatinine over 1.5 mg/dl.


Definition and of acute renal failure in cirrhosis

Conventional criteria = a rapid reduction in kidney function currently defined as a percentage increase in serum creatinine of more or equal to 50 % (1.5-fold from baseline) to a final value equal or higher than 1.5 mg/dl.


Definition and staging of Acute Kidney Injury (AKI)

**KDIGO criteria** = an abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l), or a percentage increase in serum creatinine of more or equal to 50% (1.5-fold from baseline) in less than 7 days.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1°</td>
<td>Increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l) or a percentage increase in serum creatinine of more or equal to 50% (&lt; 2 fold from baseline).</td>
</tr>
<tr>
<td>2°</td>
<td>Increase in serum creatinine to more than 200% to 300% (&gt; 2- to 3-fold) from baseline</td>
</tr>
<tr>
<td>3°</td>
<td>Increase in serum creatinine to more than 300 % (&gt; 3-fold) from baseline or serum creatinine of more 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 need for renal replacement therapy</td>
</tr>
</tbody>
</table>

Outcome according to renal status in patients with cirrhosis and bacterial infection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pts with AKI (n° = 166)</th>
<th>Pts without AKI (n° = 171)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N° of deaths</td>
<td>68 (34 %)</td>
<td>12 (7 %)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Pts transferred to ICU</td>
<td>76 (46%)</td>
<td>35 (20%)</td>
<td>&lt;0.0025</td>
</tr>
<tr>
<td>Lenght of hospital stay (days)</td>
<td>17.8 ± 19.8</td>
<td>13.3 ± 31.8</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

F. Wong et al. Gastroenterology (Epub ahead of print)
Initial AKI stage and in-hospital mortality

- No AKI: Serum creatinine < 1.5 mg/dl
- AKI stage 1
- AKI stage 2: $P < 0.0001$
- AKI stage 3: $P < 0.0001$
- In-hospital mortality: $P < 0.001$
- $P < 0.025$
- $P = N.S.$

S. Piano et al. J. Hepatol. 2013; 59: 482-489
Survival of in hospitalized patients with cirrhosis according to the AKI peak stage

AKI-1\(^\#\) = serum creatinine < 1.5 mg/dl

Accuracy of conventional criterion vs KDIGO criteria in the prediction of in-hospital mortality in a series of 233 patients with cirrhosis and ascites

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensibility 95% CI</th>
<th>Specificity 95% CI</th>
<th>PPV 95% CI</th>
<th>NPV 95% CI</th>
<th>LR+ 95% CI</th>
<th>LR- 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional criterion</td>
<td>0.5152 (0.33 - 0.69)</td>
<td>0.9450 (0.90 - 0.97)</td>
<td>0.6071 (0.40 - 0.78)</td>
<td>0.9220 (0.87 - 0.95)</td>
<td>9.3664 (4.8 - 18.17)</td>
<td>0.5131 (0.36 - 0.73)</td>
</tr>
<tr>
<td>KDIGO criteria</td>
<td>0.6667 (0.48 - 0.82)</td>
<td>0.8100 (0.74 - 0.86)</td>
<td>0.3667 (0.24 - 0.50)</td>
<td>0.9364 (0.88 - 0.96)</td>
<td>3.5088 (2.41 - 5.10)</td>
<td>0.4115 (0.25 - 0.66)</td>
</tr>
<tr>
<td>KDIGO with Progression</td>
<td>0.5455 (0.36 - 0.71)</td>
<td>0.9450 (0.90 - 0.97)</td>
<td>0.6207 (0.42 - 0.79)</td>
<td>0.9265 (0.88 - 0.95)</td>
<td>9.9174 (5.15 - 19.06)</td>
<td>0.4810 (0.33 - 0.70)</td>
</tr>
</tbody>
</table>

S. Piano et al. J. Hepatol. 2013; 59: 482-489
Characteristics of patients according to progression of initial stage of AKI

<table>
<thead>
<tr>
<th></th>
<th>Non-progressors (n° = 37)</th>
<th>Progressors (n° = 16)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) – mean (SD)</td>
<td>67.4 (10.6)</td>
<td>70.4 (7)</td>
<td>0.3707</td>
</tr>
<tr>
<td>Gender M/F – n° (%)</td>
<td>20 (54%) / 17 (46%)</td>
<td>8 (50%) / 8 (50%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Child Pugh score – median (min-max)</td>
<td>10 (5-14)</td>
<td>10.5 (5-14)</td>
<td>0.9286</td>
</tr>
<tr>
<td>MELD score – median (min-max)</td>
<td>19 (9-38)</td>
<td>21 (11-37)</td>
<td>0.5540</td>
</tr>
<tr>
<td>Albumin (g/dl) – median (min-max)</td>
<td>2.7 (1.9-4.3)</td>
<td>2.7 (1.8-4.5)</td>
<td>0.8824</td>
</tr>
<tr>
<td>Bilirubin (µmol/L) – median (min-max)</td>
<td>63.3 (7.9-477.8)</td>
<td>85.3 (8.9-631)</td>
<td>0.5571</td>
</tr>
<tr>
<td>Protrombin time (%) – mean (SD)</td>
<td>45.3 (13.9)</td>
<td>48.4 (16.0)</td>
<td>0.3563</td>
</tr>
<tr>
<td>Baseline sCr (mg/dl) – median (min-max)</td>
<td>1.1 (0.48-3.0)</td>
<td>1.2 (0.7-2.9)</td>
<td>0.3090</td>
</tr>
<tr>
<td>Baseline sCr ≥ 1.5 mg/dl – n (%)</td>
<td>14 (37.8)</td>
<td>5 (31.3)</td>
<td>0.7363</td>
</tr>
<tr>
<td>sCr ≥ 1.5 mg/dl at diagnosis of AKI – n (%)</td>
<td>19 (51.4)</td>
<td>15 (93.7)</td>
<td>0.0041</td>
</tr>
<tr>
<td>Bacterial infections – n (%)</td>
<td>24 (64.9)</td>
<td>11 (68.8)</td>
<td>1.000</td>
</tr>
<tr>
<td>Leukocyte counts el/µl – median (min-max)</td>
<td>6,500 (1,240-18,480)</td>
<td>6,170 (2,750-13,570)</td>
<td>0.9764</td>
</tr>
</tbody>
</table>
Survival in patients without AKI (Controls) and with AKI and a final serum creatinine value ≤ 1.5 mg/dl (Group A) or a serum creatinine > 1.5 mg/dl (Group B)

- Controls: n = 171
- Group A: n = 31
- Group B: n = 135

F. Wong et al. J. Hepatol. 2015; 62: 739-752
Algorithm for AKI management in patients with cirrhosis

Initial AKI# stage 1°

Close monitoring
Remove risk factors (withdrawal of nephrotoxic drugs, vasodilators and NSADs, taper/withdraw diuretics, expand plasma volume, treat infections* when diagnosed)

Resolution

Close follow up

Initial AKI# stage > 1°

#= AKI at the first fulfilling of KDIGO criteria

P. Angeli et al. J. Hepatol. 2015; 62: 968-974
Survival in patients with cirrhosis according to the occurrence of transient AKI

Algorithm for AKI management in patients with cirrhosis

Initial AKI# stage 1°
- Close monitoring
- Remove risk factors (withdrawal of nephrotoxic drugs, vasodilators and NSADs, taper/withdraw diuretics, expand plasma volume, treat infections* when diagnosed)

Resolution
- Close follow up

Persistance
- Further treatment of AKI decided on a case-by-case basis

Progression
- Yes: Specific treatment for other AKI phenotypes
- No: Does AKI Meet criteria of HRS?
  - No: Withdrawal of diuretics (if not yet applied) and volume expansion with albumin (1g/kg) for 2 days
  - Yes: vasoconstrictors and albumin

Initial AKI# stage > 1°
- Withdrawal of diuretics (if not yet applied) and volume expansion with albumin (1g/kg) for 2 days

Response?
- Yes
- No

# = AKI at the first fulfilling of KDIGO criteria

P. Angeli et al. J. Hepatol. 2015; 62: 968-974
Clinical consequences of the new algorithm for AKI management in patients with cirrhosis (1)

- The acceptance of the main point that derived from the application of KDIGO criteria that is to focus attention on and to manage promptly even small increases in serum creatinine

- A more rationale application of the therapeutic resources

_P. Angeli et al. J. Hepatol. 2015 ; 62 : 968-974_
Definition and staging of Acute Kidney Injury (AKI)

**KDIGO urine output criteria** = an urinary output < 0.5 ml/kg B.W./hr x 6-12 hours

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1°</td>
<td>an urinary output &lt; 0.5 ml/kg B.W./hr x 6-12 hours</td>
</tr>
<tr>
<td>2°</td>
<td>an urinary output &lt; 0.5 ml/kg B.W./hr x 12 hours</td>
</tr>
<tr>
<td>3°</td>
<td>an urinary output &lt; 0.5 ml/kg B.W./hr x 24 hours or anuria per 12 hr</td>
</tr>
</tbody>
</table>

Patient classification by KDIGO criteria

- Patients: 75
- AKI sCr or UO: 45
- AKI only sCr: 4
- AKI sCr and UO: 17
- AKI only UO: 24

Adapted from E. Macedo Nephrol. Dial. Transplant 2011; 26: 509-515
Relationship between nº of hours of oliguria in ICU and hospital mortality

E. Macedo Nephrol. Dial. Transplant 2011; 26: 509-515 (modified)
Relationship between combination of UO and sCr criteria an survival

Group 1 (green), no AKI by either criterion;
Group 2 (blue), stages 1–2 by UO criteria but no AKI by SC or stage 1 by SC and no AKI by UO;
Group 3 (yellow), stages 1–2 by UO plus stage 1 by SC or stages 2–3 by SC alone;
Group 4 (orange), stages 1–2 by UO plus stage 2 by SC or stage 3 by UO alone;
Group 5 (red), stage 3 by UO plus stages 1–2 by SC or stage 3 by SC plus stages 1–2 by UO;
Group 6 (dark red), stage 3 by both criteria.

*J.A. Kellum et al. J. Am. Soc. Nephrol. 2015; 26: 2231-2238*
Definition and defining criteria of AKI in cirrhosis

Table 2. International Club of Ascites (ICA-AKI) new definitions for the diagnosis and management of AKI in patients with cirrhosis.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline sCr</td>
<td>A value of sCr obtained in the previous 3 months, when available, can be used as baseline sCr. In patients with more than one value within the previous 3 months, the value closest to the admission time to the hospital should be used. In patients without a previous sCr value, the sCr on admission should be used as baseline.</td>
</tr>
<tr>
<td>Definition of AKI</td>
<td>• Increase in sCr ≥0.3 mg/dl (≥26.5 μmol/L) within 48 hours; or,</td>
</tr>
<tr>
<td></td>
<td>• A percentage increase sCr ≥50% from baseline which is known, or presumed, to have occurred within the prior 7 days</td>
</tr>
<tr>
<td>Staging of AKI</td>
<td>• <strong>Stage 1</strong>: increase in sCr ≥0.3 mg/dl (26.5 μmol/L) or an increase in sCr ≥1.5-fold to 2-fold from baseline</td>
</tr>
<tr>
<td></td>
<td>• <strong>Stage 2</strong>: increase in sCr &gt;2-fold to 3-fold from baseline</td>
</tr>
<tr>
<td></td>
<td>• <strong>Stage 3</strong>: increase of sCr &gt;3-fold from baseline or sCr ≥4.0 mg/dl (353.6 μmol/L) with an acute increase ≥0.3 mg/dl (26.5 μmol/L) or initiation of renal replacement therapy</td>
</tr>
<tr>
<td>Progression of AKI</td>
<td><strong>Progression</strong></td>
</tr>
<tr>
<td></td>
<td>Progression of AKI to a higher stage and/or need for RRT</td>
</tr>
<tr>
<td></td>
<td><strong>Regression</strong></td>
</tr>
<tr>
<td></td>
<td>Regression of AKI to a lower stage</td>
</tr>
<tr>
<td>Response to treatment</td>
<td><strong>No response</strong></td>
</tr>
<tr>
<td></td>
<td>No regression of AKI</td>
</tr>
<tr>
<td></td>
<td><strong>Partial response</strong></td>
</tr>
<tr>
<td></td>
<td>Regression of AKI stage with a reduction of sCr to ≥0.3 mg/dl (26.5 μmol/L) above the baseline value</td>
</tr>
<tr>
<td></td>
<td><strong>Full response</strong></td>
</tr>
<tr>
<td></td>
<td>Return of sCr to a value within 0.3 mg/dl (26.5 μmol/L) of the baseline value</td>
</tr>
</tbody>
</table>

AKI, acute kidney injury; RRT, renal replacement therapy; sCr, serum creatinine.

*P. Angeli et al. Gut 2015; 64: 531-537*
### Definition of Kidney Disease

<table>
<thead>
<tr>
<th>Definition</th>
<th>Functional criteria</th>
<th>Structural criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AKI</strong></td>
<td>Increase in sCr by 50% within 7 days or increase in sCr by 0.3 mg/dl within 2 days</td>
<td>No criteria</td>
</tr>
<tr>
<td><strong>AKD</strong></td>
<td>AKI or GFR &lt; 60 ml/min per 1.73 m² for &lt; 3 months</td>
<td>Kidney damage for &lt; 3 months</td>
</tr>
<tr>
<td></td>
<td>Decrease in GFR ≥ 35% or increase in sCr ≥ 50% for &lt; 3 months</td>
<td>Kidney damage for &lt; 3 months</td>
</tr>
<tr>
<td><strong>CKD</strong></td>
<td>GFR &lt; 60 ml/min per 1.73 m² for &gt; 3 months</td>
<td>Kidney damage for ≥ 3 months</td>
</tr>
</tbody>
</table>

Definition of Kidney Disease

AKI defined as an increase in sCr ≥ 50% within 3 months

P. Angeli et al. Gut 2015; 64: 531-537
The problem of the baseline serum creatinine in the KDIGO criteria

- The KDIGO guidelines suggest that patients should be assumed to have a baseline eGFR of 75 ml/min/1.73 m² in cases where there is no history of CKD and baseline kidney function is unknown.

- The KDIGO guidelines suggest to use an inverse application of MDRD equation assuming that baseline glomerular filtration rate is 75 ml/min per 1.73 m² to calculate an imputed baseline creatinine.

Estimated Glomerular Filtration Rate (GFR) by serum creatinine-based equations versus measured GFR

Stage 5
Stage 4
Stage 3
Stage 2
Stage 1

S. Rosi et al. Liver Int. 2015; (Epub ahead of print)
The problem of the baseline serum creatinine in the KDIGO criteria

Patient with cirrhosis

Age = 65 yrs
Gender: male
Race: African American
mGFR = 75 ml/min/1.73 m²
sCr = 0.9 mg/dl

eGFR = 75 ml/min 1.73 m² in MDRD formula = imputed value of sCr of 1.24 mg/dl

S. Rosi et al. Liver Int. 2015; (Epub ahead of print)
Prevalence of AKI on admission using an imputed value or a previous value of serum creatinine (sCr)

$p < 0.05$

S. Rosi et al. Liver Int. 2015; (Epub ahead of print)
Phenotypes of AKI in patients with cirrhosis and ascites

- Acute tubular necrosis (ATN-AKI) (41.7%)
- Prerenal failure (Prenal-AKI) (38%)
- Hepatorenal syndrome (HRS-AKI) (20%)
- Postrenal failure (Postrenal AKI) (0.3%)

Current diagnostic criteria of HRS

1. Cirrhosis with ascites;

2. Serum creatinine > 133 µmol/l (1.5 mg/dl);

3. No sustained improvement of serum creatinine (decrease to a level of 133 µmol/l or less) after at least two days of diuretic withdrawal and volume expansion with albumin. The recommended dose of albumin is 1 g/kg of body weight per day to a maximum of 100 g/day;

4. Absence of shock

5. No current or recent treatment with nephrotoxic drugs;

6. Absence of parenchimal disease as indicated by proteinuria >500 mg/day, microhematuria (>50 red blood cells per high power field) and/or abnormal renal ultrasonography.

Values of urinary biomarkers in patients categorized according to the absence or presence of AKI and phenotype of AKI

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>No AKI</th>
<th>Prerenal AKI</th>
<th>HRS-AKI</th>
<th>ATN-AKI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NGAL (μg/g sCr)</td>
<td>30 (17-41)</td>
<td>36 (26-125)</td>
<td>104 (58-208)</td>
<td>1807 (494-3716)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IL-18 (ng/g sCr)</td>
<td>21 (16-35)</td>
<td>16 (14-36)</td>
<td>18 (10-29)</td>
<td>150 (58-259)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Albumin (mg/g sCr)</td>
<td>3 (1-7)</td>
<td>9 (1-77)</td>
<td>16 (8-46)</td>
<td>324 (53-380)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TFF-3 (μg/g sCr)</td>
<td>582 (367-1665)</td>
<td>2300 (323-2720)</td>
<td>1893 (840-2715)</td>
<td>5810 (4019-14466)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MCP-1 (μg/g sCr)</td>
<td>0.2 (0.1-1.4)</td>
<td>0.9 (0.2-2.5)</td>
<td>3 (1-6)</td>
<td>4 (1-14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Osteopontin (μg/g sCr)</td>
<td>1456 (715-3210)</td>
<td>2914 (1847-8382)</td>
<td>5471 (2959-11983)</td>
<td>83337 (4019-14466)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calbindin (μg/g sCr)</td>
<td>71 (26-150)</td>
<td>5 (2-34)</td>
<td>25 (8-58)</td>
<td>118 (37-324)</td>
<td>0.010</td>
</tr>
<tr>
<td>GST-TT (μg/g sCr)</td>
<td>3 (1-16)</td>
<td>3 (1-7)</td>
<td>4 (2-21)</td>
<td>50 (9-169)</td>
<td>0.012</td>
</tr>
<tr>
<td>KIM-1 (μg/g sCr)</td>
<td>0.5 (0.3-1.4)</td>
<td>0.5 (0.1-1.1)</td>
<td>1.2 (0.5-2.8)</td>
<td>1.7 (0.9-5.1)</td>
<td>0.015</td>
</tr>
<tr>
<td>Cistatin C (μg/g sCr)</td>
<td>24 (12-435)</td>
<td>21 (15-53)</td>
<td>27 (10-47)</td>
<td>115 (39-1552)</td>
<td>0.023</td>
</tr>
</tbody>
</table>

X. Ariza et al. Plos One 2015 ; 10 [Epub ahead of print]
Percentage of patients with prerenal- (PRE-), hepatorenal syndrome (HRS-), and acute tubular necrosis- (ATN-) AKI by the number of biomarkers of structural injury above their optimal cutoff for the diagnosis of ATN.

*JM. Belcher et al. Hepatology 2014 ; 60 : 622-632*
Pharmacologic therapy for HRS

- Albumin (20-40 g/day intravenously)
- Terlipressin (0.5-2 mg/4-6hr intravenously)

Rate of response in patients with type 1 HRS according to the schedule of i.v. administration of terlipressin

<table>
<thead>
<tr>
<th></th>
<th>Complete response</th>
<th>Partial response</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.V. Continuous Infusion</td>
<td>55.88%</td>
<td>20.59%</td>
</tr>
<tr>
<td>I.V. Boluses</td>
<td>45.95%</td>
<td>18.9%</td>
</tr>
</tbody>
</table>

P = N.S.

M. Cavallin et. al. 2016; 63: 983-992
Clinical types

**Type 1 HRS**: rapidly progressive reduction of renal function as defined by a doubling of the initial serum creatinine to a level $> 226 \, \mu\text{mol/l}$ or 2.5 mg/dl in less than two weeks. It may occur spontaneously, but it can also follow a precipitating event.

Clinical pattern: acute renal failure

**Type 2 HRS**: is characterized by moderate renal failure (serum creatinine from 133 to 226 $\mu\text{mol/l}$ or 1.5 to 2.5 mg/dl) with a steady or slowly progressive course.

Clinical pattern: refractory ascites

Response to treatment according to the baseline serum creatinine value

### Relationship between MAP and serum creatinine (SCr) in HRS

<table>
<thead>
<tr>
<th>Baseline SCr</th>
<th>Required SCr to achieve goal (%)</th>
<th>Predicted increase in MAP to achieve SCr goal (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>1.5 (25%)</td>
<td>3.7 (2.5-4.9)</td>
</tr>
<tr>
<td>3.0</td>
<td>1.5 (30%)</td>
<td>8.5 (6.7-10.3)</td>
</tr>
<tr>
<td>4.0</td>
<td>1.5 (62.5%)</td>
<td>13.3 (10.3-16.3)</td>
</tr>
</tbody>
</table>

*J.C. Q. Velez et al. Am. J. Kidney Dis. 2011; 58: 928-938*
Clinical types

HRS-AKI

**Type 2 HRS:** is characterized by moderate renal failure (serum creatinine from 133 to 226 µmol/l or 1.5 to 2.5 mg/dl) with a steady or slowly progressive course.

Clinical pattern: refractory ascites

Algorithm for AKI management in patients with cirrhosis

Initial AKI# stage 1°
- From 0.6 to 0.9 mg/dl
- Close monitoring
- Remove risk factors (withdrawal of nephrotoxic drugs, vasodilators and NSADs, taper/withdraw diuretics, expand plasma volume, treat infections when diagnosed)

Resolution
- Close follow up

Further treatment of AKI decided on a case-by-case basis

Persistance
- From 0.9 to 1.2 mg/dl
- Progression
- NO
- YES

Initial AKI# stage > 1°
- Withdrawal of diuretics (if not yet applied) and volume expansion with albumin (1g/kg) for 2 days
- From 1.2 to 1.4 mg/dl

Response?
- YES
- NO

Does AKI Meet criteria of HRS?
- NO
- YES
- Specific treatment for other AKI phenotypes
- Vasoconstrictors and albumin

P. Angeli et al. J. Hepatol. 2015 ; 62 : 968-974

# = AKI at the first fulfilling of KDIGO criteria
Clinical consequences of the new algorithm for AKI management in patients with cirrhosis (2)

- A more rationale application of the therapeutic resources (avoiding of potentially dangerous consequences of an overtreatment of AKI as a consequence of an uncritical application of the AKIN criteria)

- A clear distinction between AKI and hepatorenal syndrome (which is only one of the possible phenotypes of AKI)

- The definitive removal of the cut off of serum creatinine from the criteria for diagnosis and treatment of HRS in the setting of AKI (HRS-AKI).

*P. Angeli et al. on behalf of ICA, J. Hepatol. 2015 62 : 968-974*