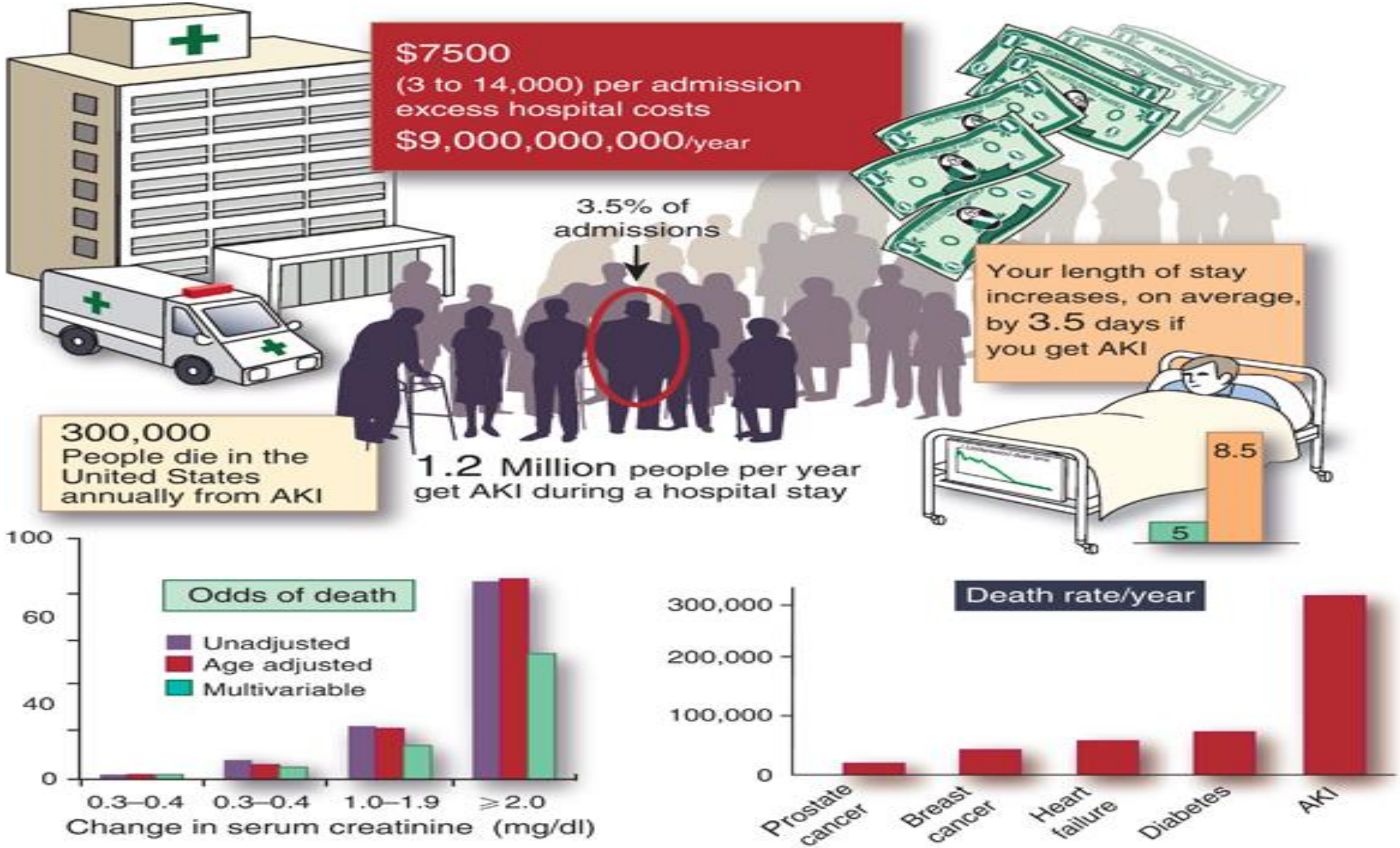
AKI in Cancer Patients

Amir A. Nassiri, M.D, D.I.U

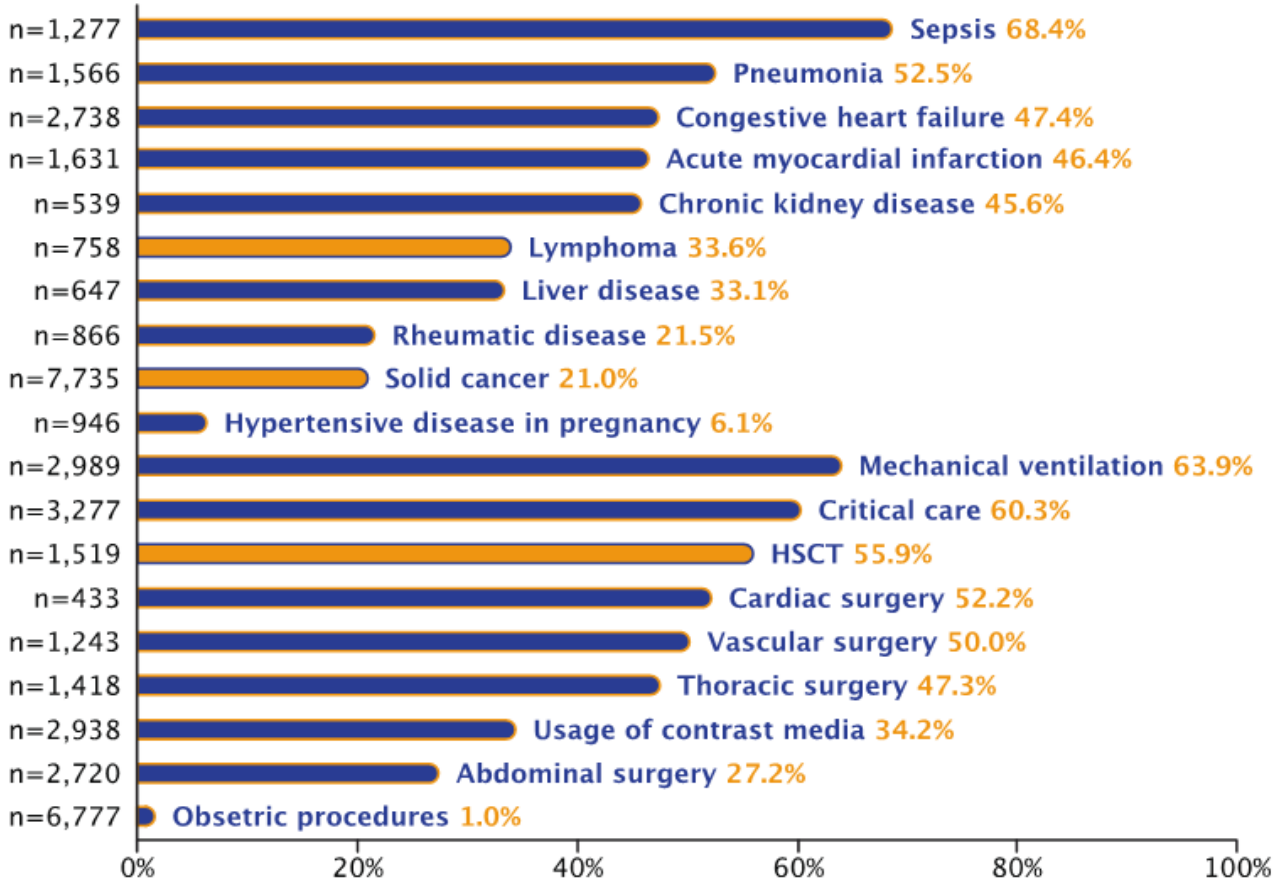
SBUMS

Tehran 2019

World Health Organization


$7500
(3 to 14,000) per admission
excess hospital costs
$9,000,000,000/year
3.5% of
admissions
Your length of stay
increases, on average,
by 3.5 days if
you get AKI
300,000
People die in the
United States
annually from AKI
1.2 Million people per year
get AKI during a hospital stay
8.5
5
100
60
40
0
Odds of death
Unadjusted
Age adjusted
Multivariable
0.3–0.4
0.3–0.4
1.0–1.9
⩾2.0
Change in serum creatinine (mg/dl)
Death rate/year
300,000
200,000
100,000
0
Prostate cancer
Breast cancer
Heart failure
Diabetes
AKI

AKI IN SETTING OF OTHER CO-MORBIDITIES



Zeng et al, CJASN 2014

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Original article

Incidence of acute kidney injury in cancer patients: A Danish population-based cohort study

Christian Fynbo Christiansen [a,*], Martin Berg Johansen [a], Wendy J. Langeberg [b], Jon P. Fryzek [b], Henrik Toft Sørensen [a]

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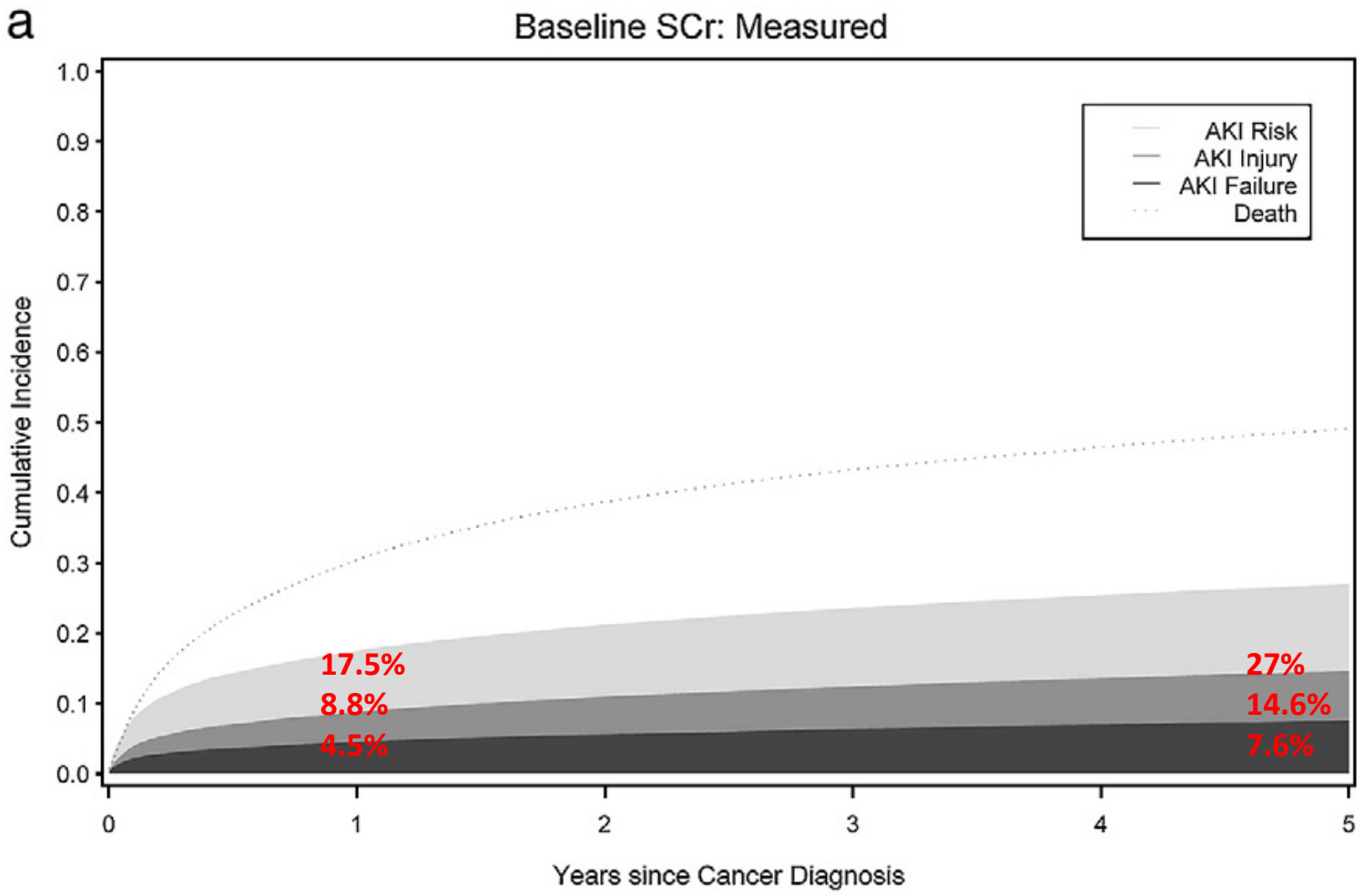
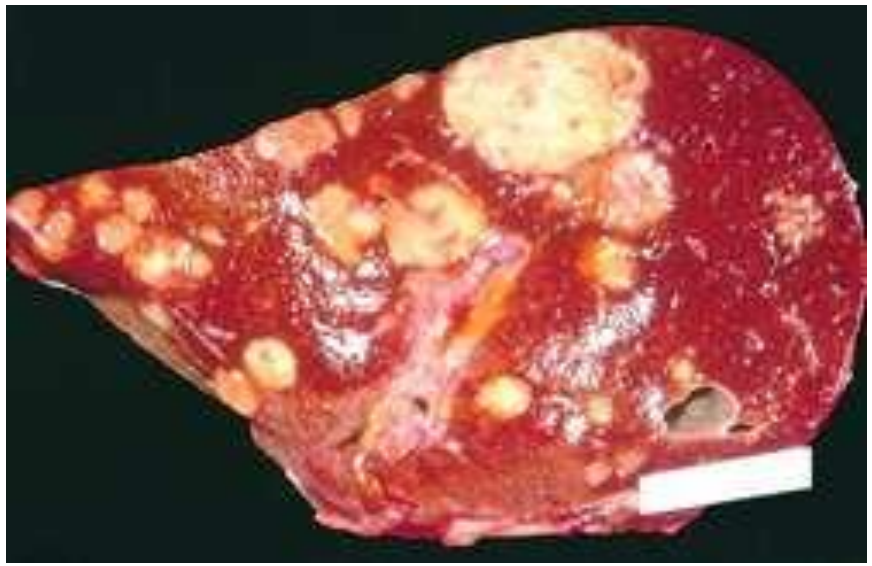
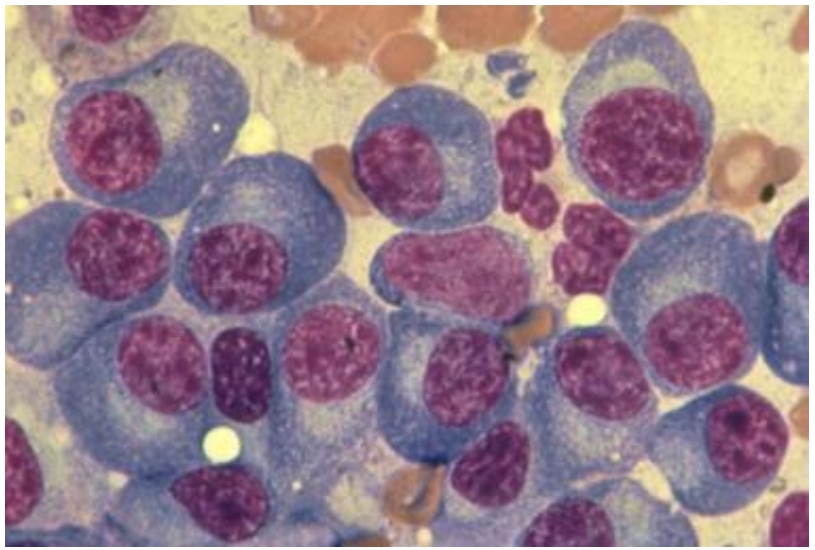
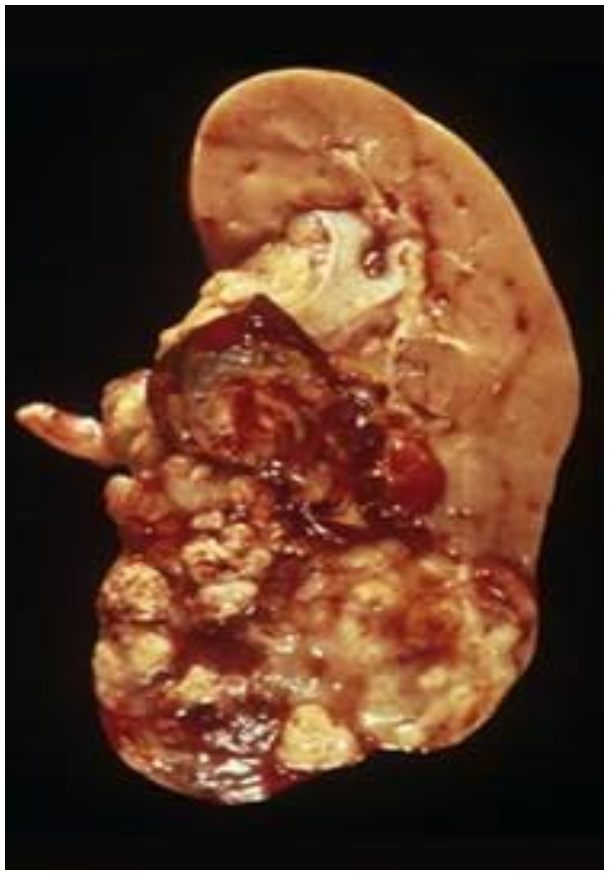
Cumulative incidence (risk) of acute kidney injury (AKI) during the first 5 years after a cancer diagnosis



Cancers with the highest 1-yr risk of AKI







Acute kidney injury in cancer patients: A nationwide survey in China

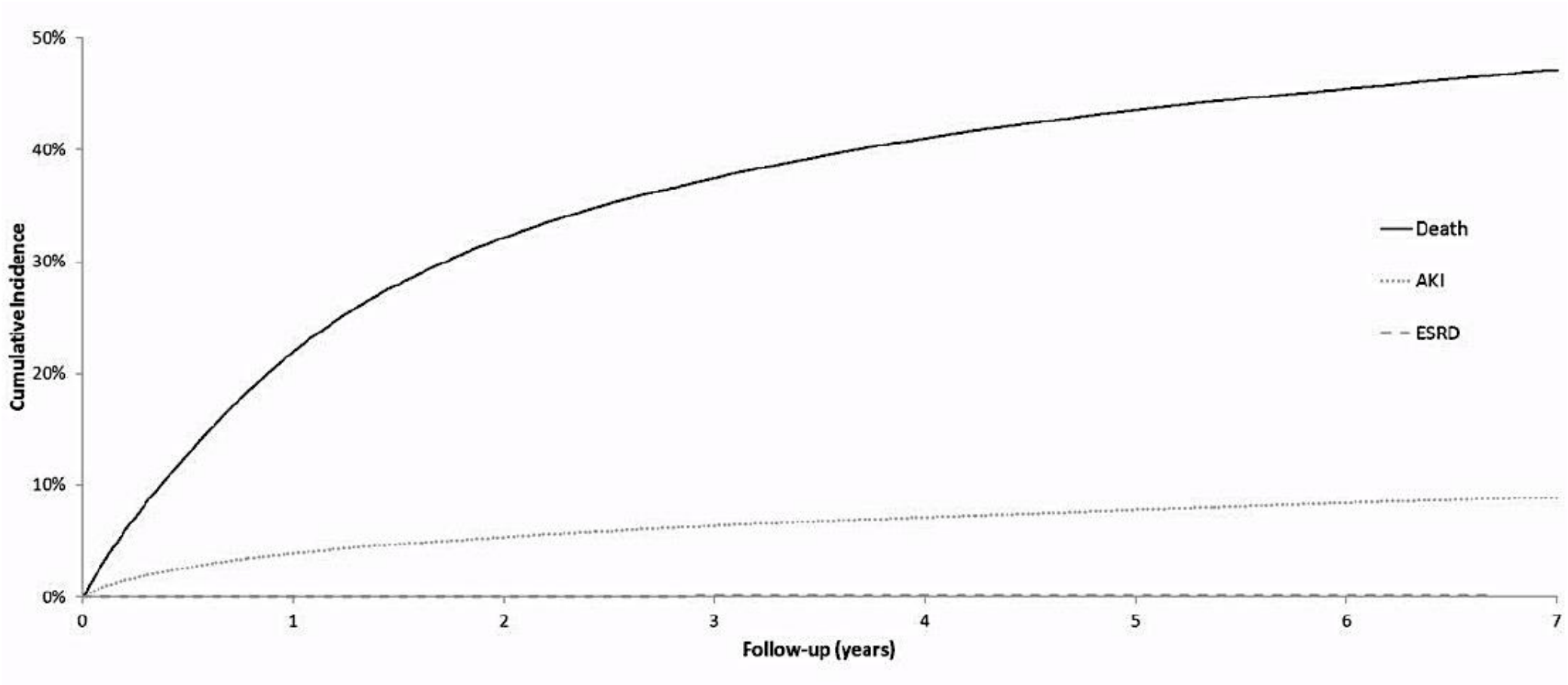
Juan Jin[1,2], Yafang Wang[3], Quanquan Shen[1,2], Jianguang Gong[1,2], Li Zhao[1,2] & Qiang He[1,2]

Cancer patients have a high risk for acute kidney injury (AKI); however, the incidence, severity, and risk factors of malignancy-related AKI (MR-AKI) are unclear. This study aimed to assess MR-AKI risk factors and provide reliable data for AKI prevention, diagnosis, and management in China. This cross-sectional study analysed data from 44 academic and local hospitals in China. AKI patients were identified based on 2 screening criteria: the 2012 Kidney Disease: Improving Global Outcomes-AKI definition and the expanded screening criteria for patients with no repeated serum creatinine (SCr) test within 7 days and those who recovered from AKI. Patients whose SCr level increased or decreased by 50% during hospitalization, compared with that at admission, were considered to have AKI according to the expanded criteria. A total of 7,604 AKI patients were enrolled (1,418 with MR-AKI). Patient characteristics were compared between the MR-AKI and non-MR-AKI groups. Multivariate logistic models were used to statistically assess risk factors. The proportions of MR-AKI patients in academic and local hospitals were 20.2% and 14.1%, respectively. The incidence of MR-AKI was higher in mid-China (the affluent region), elderly patients, and groups with higher per capita gross domestic product. Among MR-AKI cases, gastrointestinal cancer (50.1%) was the most common malignancy, followed by cancers of the reproductive (15.3%), haematological (13.1%), respiratory (11.8%), and other systems (8.3%), and cancers of unknown classification (1.4%). Of 268 hospital deaths, respiratory, haematological, gastrointestinal, reproductive, other system, and unknown classification cancers accounted for 29.3%, 18.8%, 18.6%, 12.9%, 16.9%, and 20.0%, respectively. Increased age, advanced AKI stage at peak, level of per capita gross domestic product, geographic region, and renal replacement therapy indication were risk factors for hospital mortality in patients with gastrointestinal MR-AKI, whereas cardiovascular disease history, AKI stage at peak, and geographic region were risk factors for mortality in patients with reproductive MR-AKI. The incidence and mortality of MR-AKI vary by hospital, economic level, age, geographic region, and malignancy type. High MR-AKI incidence was associated with gastrointestinal cancers and higher level of medical care provided by academic hospitals in affluent regions such as Beijing, Shanghai, and other provincial-level cities. Elderly patients with advanced gastrointestinal cancer in mid-China showed the highest incidence of MR-AKI and in-hospital mortality, and thus require special attention.

AKI is common among cancer patients

- Ontario, Canada: 163,071 patients undergoing cancer therapy between 2007-2014
- One in 10 developed **AKI-D** or required **hospitalization**
- **Annual incidence of AKI** increased from 18 to 52 per 1000 person years
- Highest AKI incidence with myeloma (26%), bladder cancer (19%), leukemia (15%), and kidney cancer (14%)

2007-2014



Kitchlu A, et al. J Natl Cancer Inst 2018

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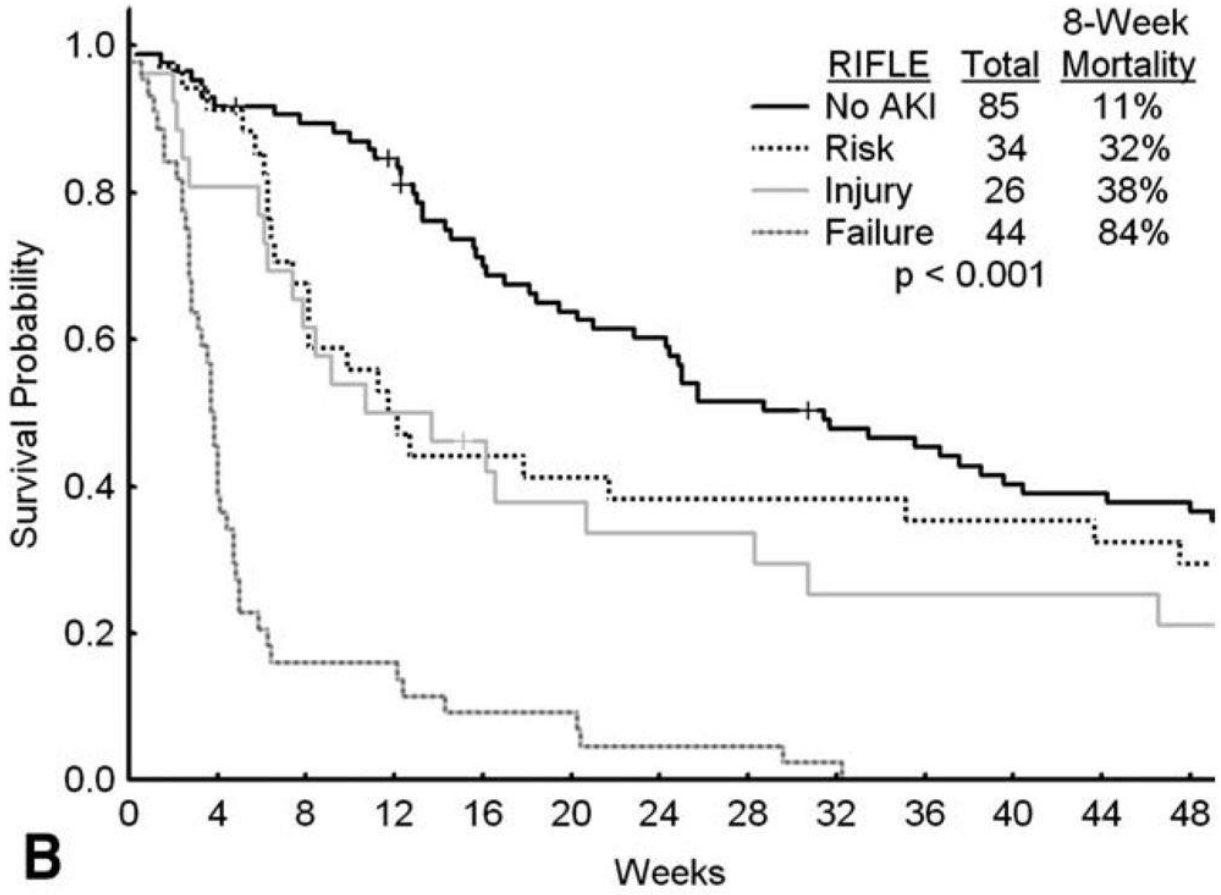
Predictors and Outcome of Acute Kidney Injury in Patients With Acute Myelogenous Leukemia or High-Risk Myelodysplastic Syndrome

Amit Lahoti, MD[1], **Hagop Kantarjian, MD**[2], **Abdulla K. Salahudeen, MD**[1], **Farhad Ravandi, MD**[2], **Jorge E. Cortes, MD**[2], **Stefan Faderl, MD**[2], **Susan O'Brien, MD**[2], **William Wierda, MD**[2], and **Gloria N. Mattiuzzi, MD**[2]

Kaplan-Meier estimates of patient survival stratified by disease response: (B) no complete remission.

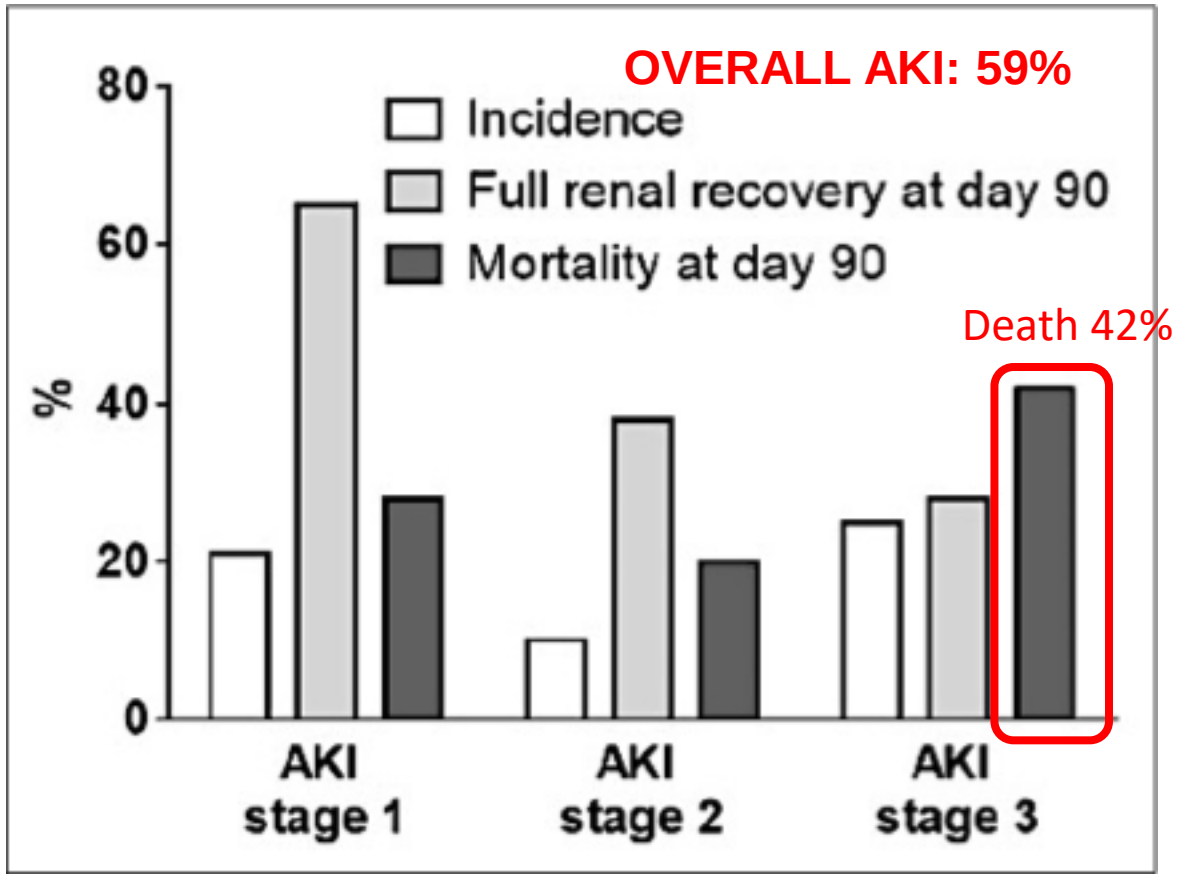


Kaplan-Meier Estimates of 8-Week Mortality by RIFLE Category

	Initial Cr[a]	Maximum Cr[a]	No. of Patients (%)	8-Week Mortality	95% CI
No AKI	0.9	1.0	345 (64)	3.8%	2.2–6.4%
RIFLE–Risk	0.9	1.5	81 (15)	13.6%	7.8–23%
RIFLE–Injury	0.8	1.8	51 (10)	19.6%	11–33%
RIFLE-Failure	0.9	3.0	60 (11)	61.7%	50–74%

AKI in Hospitalized ICU Patients: Solid Tumors

2011-2015



Kemlin D, et al. NDT, 2018

VOLUME 24 · NUMBER 24 · AUGUST 20 2006

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prognosis of Critically Ill Patients With Cancer and Acute Renal Dysfunction

Márcio Soares, Jorge I.F. Salluh, Marilia S. Carvalho, Michael Darmon, José R. Rocco, and Nelson Spector

From the Intensive Care Unit, Instituto Nacional de Câncer; Intensive Care Unit, Hospital Barra D'Or, Rio de

ABSTRACT

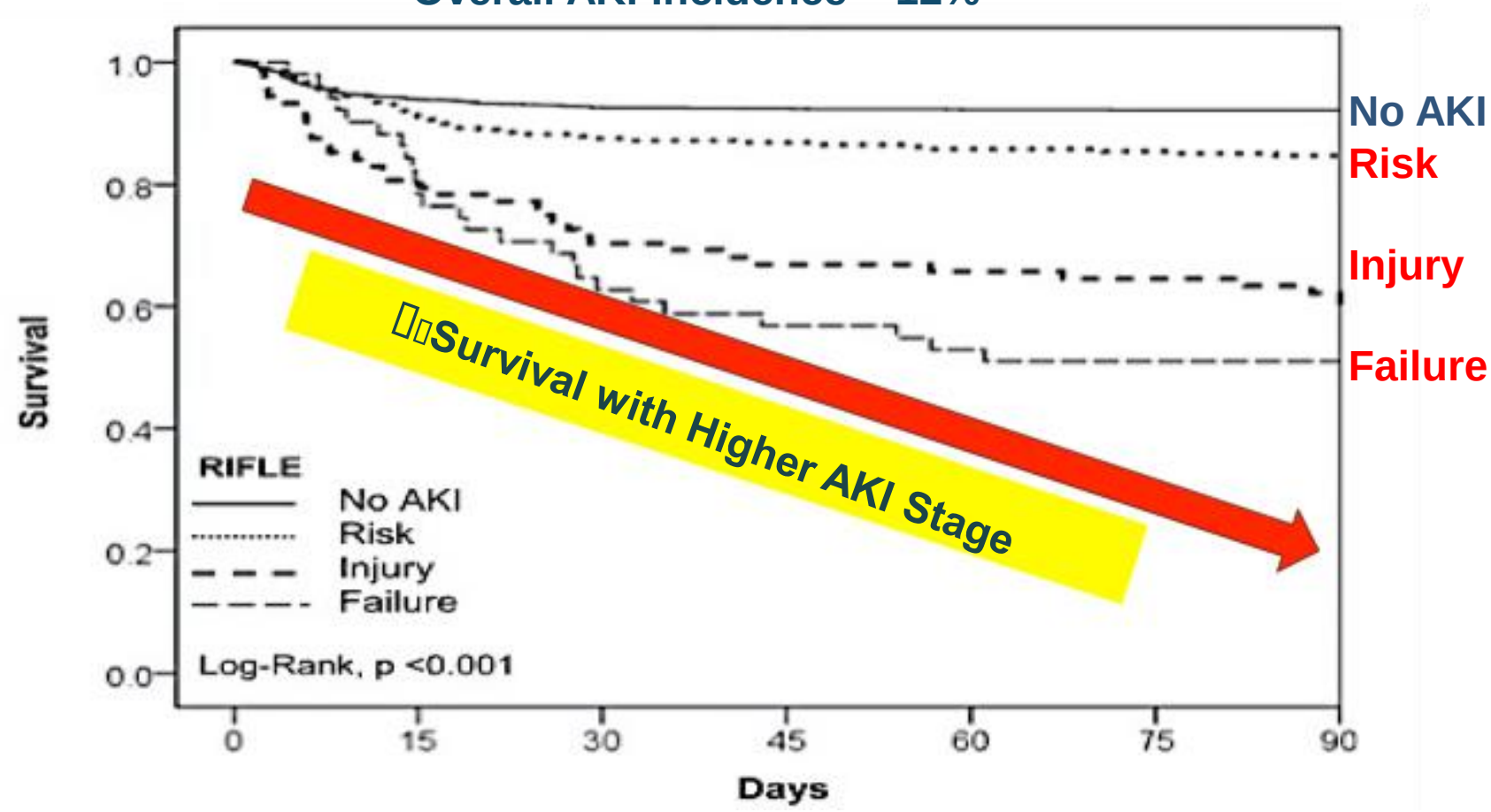
Table 4. Univariable and Multivariable Analyses of Factors Associated With 6-Month Mortality (N = 309)

Variables	6-Month Mortality (%)	Hazard Ratio	95% CI	*P*	Hazard Ratio	95% CI	*P*
Age, years							
<60	70	1.00		.463	1.00		
>60	75	1.11	0.85 to 1.44		1.36	1.00 to 1.84	.049
Sex							
Female	73	1.00		.643	—		
Male	73	0.94	0.72 to 1.23		—		
Type of cancer							
Locoregional solid tumor	66	1.00		.009	—		
Metastatic solid tumor	75	1.57	1.10 to 2.22		—		
Low-grade hematologic malignancy	84	1.40	0.88 to 2.24		—		
High-grade hematologic malignancy	88	1.65	1.17 to 2.34		—		
Performance status							
0-1	61	1.00		< .001	1.00		
2-4	85	2.05	1.57 to 2.67		1.66	1.22 to 2.26	.001
Cancer status							
Controlled	60	1.00		< .001	1.00		
Uncontrolled newly diagnosed	81	1.81	1.33 to 2.47		1.45	1.00 to 2.11	.049
Uncontrolled recurrence/progression	92	2.43	1.76 to 3.37		1.61	1.10 to 2.11	.015
Neutropenia							
No	71	1.00		< .001	—		
Yes	89	1.96	1.35 to 2.84		—		
Weight loss							
No	71	1.00		.001	—		
Yes	93	2.05	1.37 to 3.07		—		
Severe comorbidity (ACE-27)							
No	72	1.00		.234	—		
Yes	81	1.31	0.84 to 2.03		—		
Mechanical ventilation							
No	38	1.00		< .001	—		
Yes	83	3.82	2.53 to 5.76		—		
Number of associated organ failures							
0	33	1.00		< .001	1.00		
1	65	2.74	1.58 to 4.75		1.75	0.88 to 3.50	.110
2	80	4.41	2.66 to 7.32		3.24	1.62 to 6.51	< .001
≥ 3	93	6.07	3.74 to 9.87		4.07	1.94 to 8.54	< .001
Sepsis							
No	53	1.00		< .001	—		
Yes	85	2.26	1.68 to 3.04		—		
Acute on chronic renal dysfunction							
No	74	1.00		.062	—		
Yes	54	0.49	0.23 to 1.04		—		
Worsening of renal function during ICU stay							
No	70	1.00		.042	—		
Yes	85	1.39	1.01 to 1.91		—		
Oliguria							
No	72	1.00		.247	—		
Yes	74	1.17	0.90 to 1.53		—		
Classification of acute renal dysfunction							
Acute renal injury	66	1.00		.004	1.00		
Acute renal failure syndrome	80	1.73	1.25 to 2.38		1.77	1.26 to 2.49	.001
Severe acute renal failure syndrome	76	1.30	0.95 to 1.78		1.16	0.81 to 1.67	.420

Abbreviations: ACE, Adult Comorbidity Evaluation; ICU, intensive care unit.

Increased Mortality with AKI

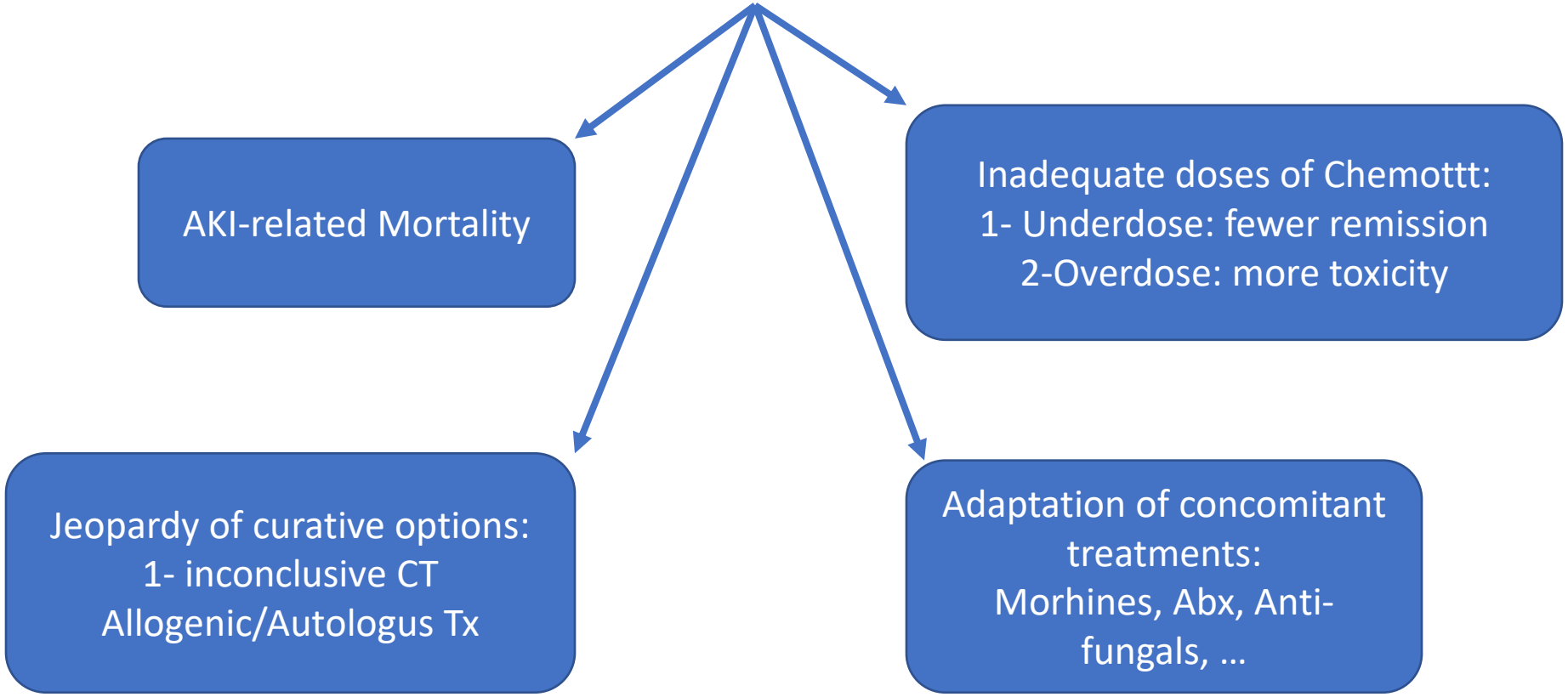
Overall AKI Incidence = 12%



Salahudeen A, et al. CJASN 2013

AKI is probably the **most common form** of renal disease
for which a **nephrologist would be consulted**
in a hospitalized **patient with cancer**.

Prognosis of Cancer pts:
Why AKI has a negative impact ?



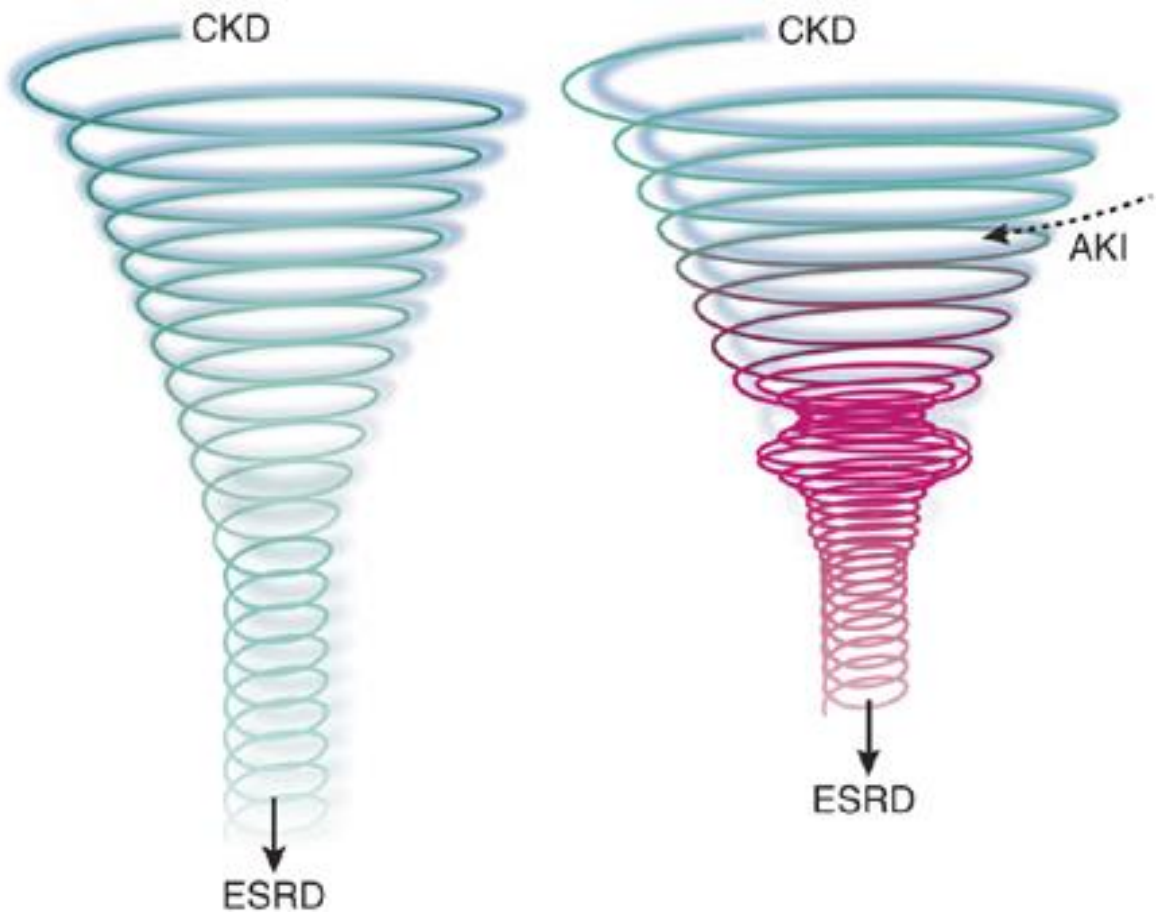
AKI + Cancer Epidemiology

- AKI is frequent in pts with cancer (up to 30%)

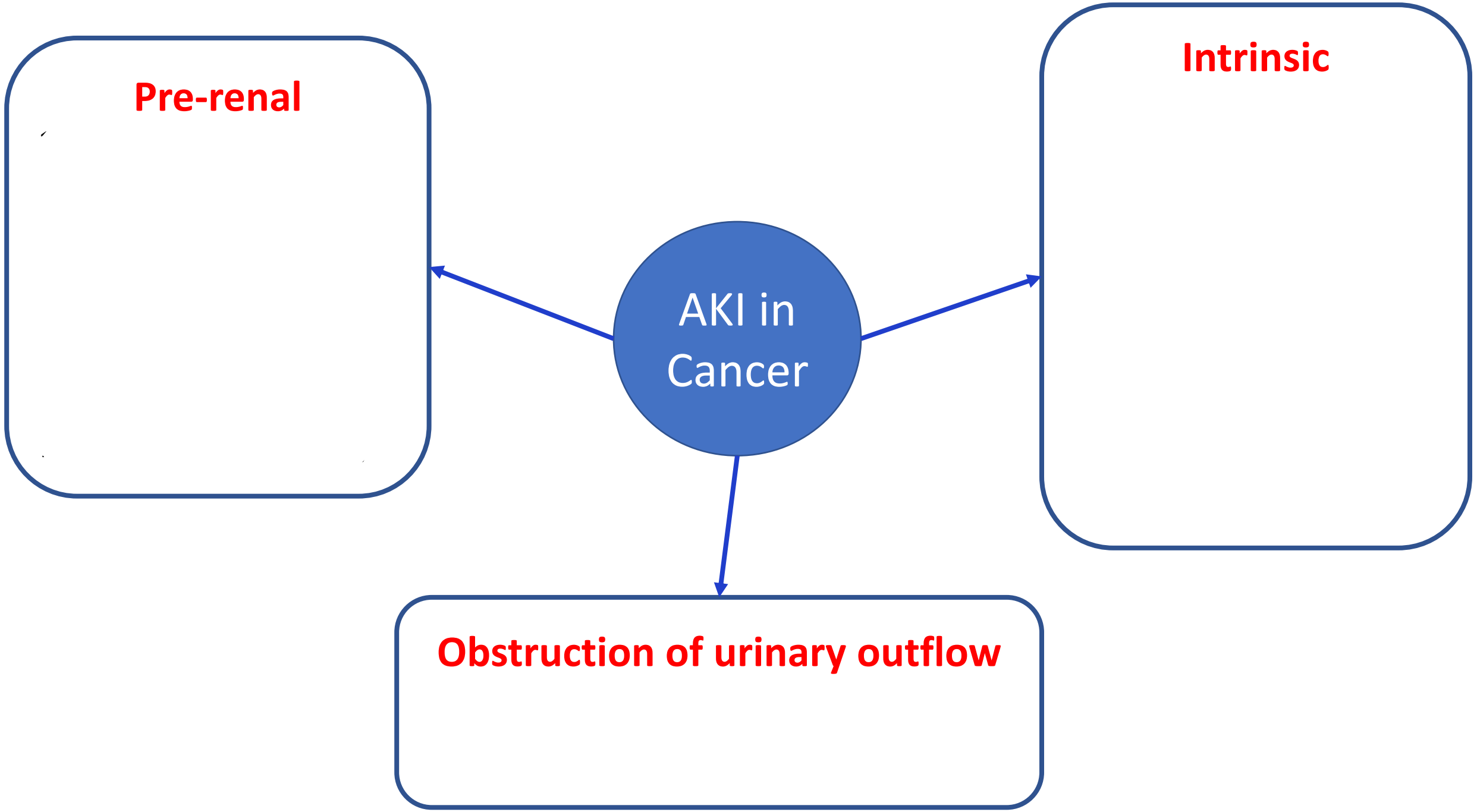
- AKI strongly worsens the prognosis of cancer pts.

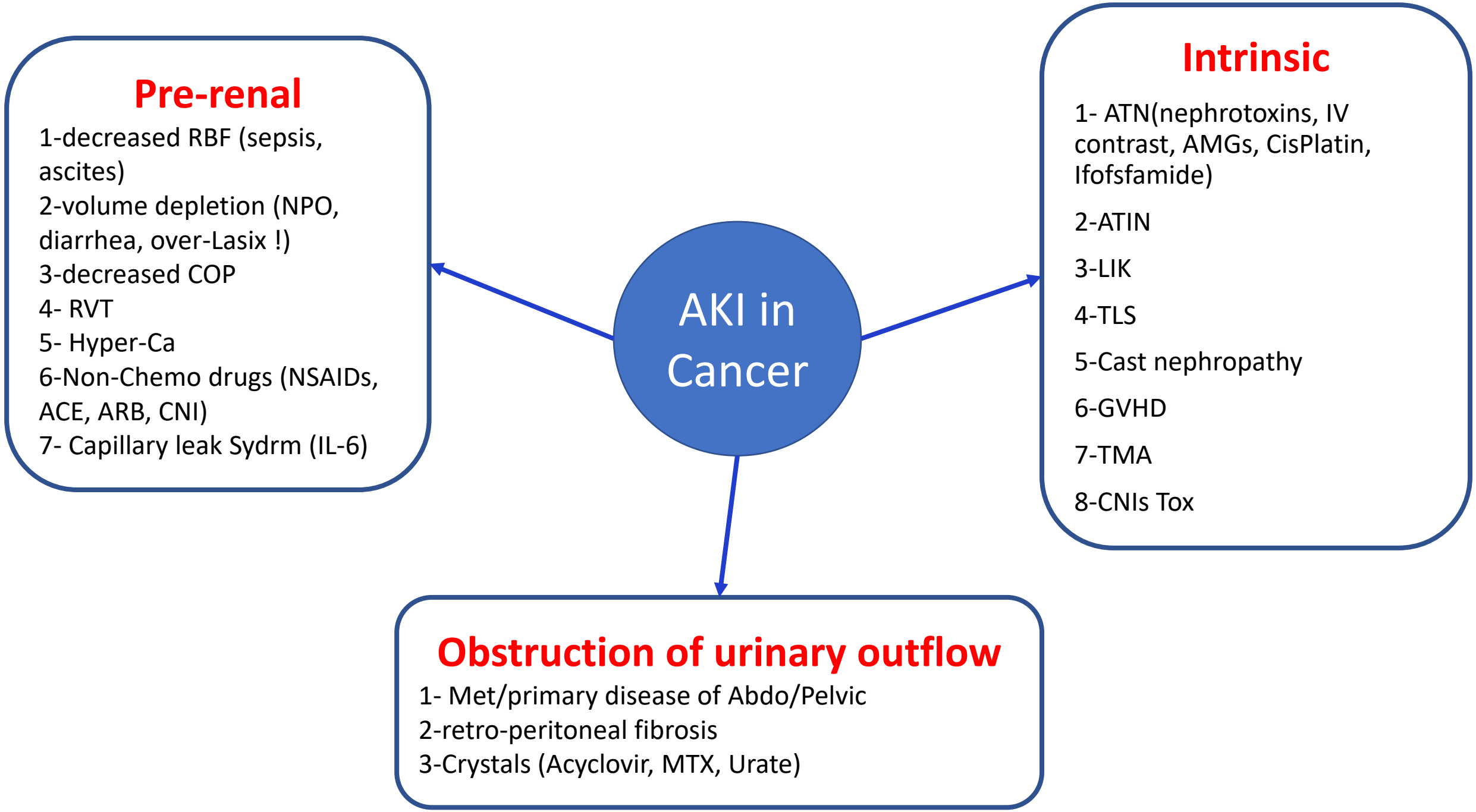
- Prognosis is related to:
- 1- severity of AKI
- 2- number of organ dysfunctions
- 3- cancer progression
- 4- age
- 5- performance status

AKI Increases the risk of progression to ESRD



Hsu et al, CJASN 2009


Pre-renal
Intrinsic
AKI in Cancer
Obstruction of urinary outflow

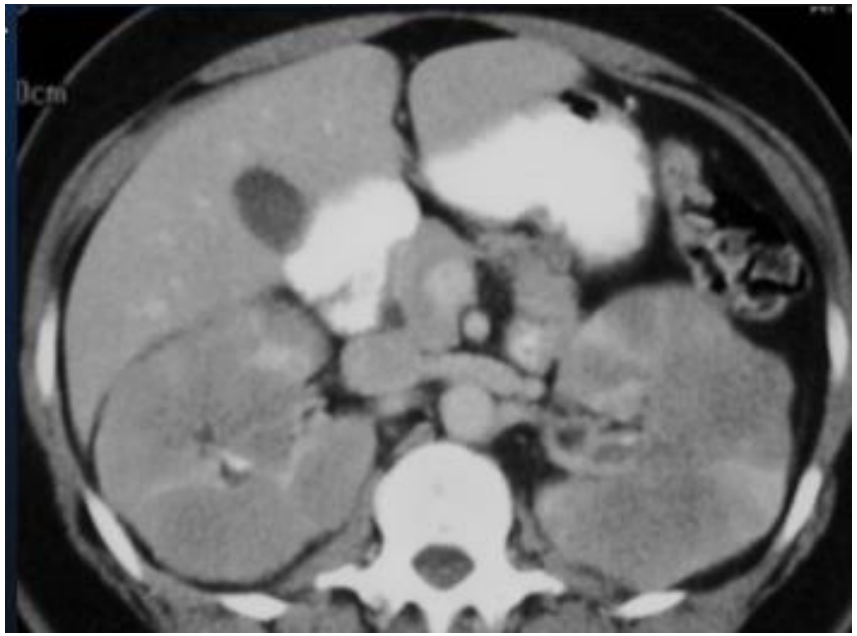

Pre-renal
1-decreased RBF (sepsis, ascites)
2-volume depletion (NPO, diarrhea, over-Lasix !)
3-decreased COP
4- RVT
5- Hyper-Ca
6-Non-Chemo drugs (NSAIDs, ACE, ARB, CNI)
7- Capillary leak Sydrm (IL-6)
AKI in Cancer
Intrinsic
1- ATN(nephrotoxins, IV contrast, AMGs, CisPlatin, Ifofsfamide)
2-ATIN
3-LIK
4-TLS
5-Cast nephropathy
6-GVHD
7-TMA
8-CNIs Tox
Obstruction of urinary outflow
1- Met/primary disease of Abdo/Pelvic
2-retro-peritoneal fibrosis
3-Crystals (Acyclovir, MTX, Urate)

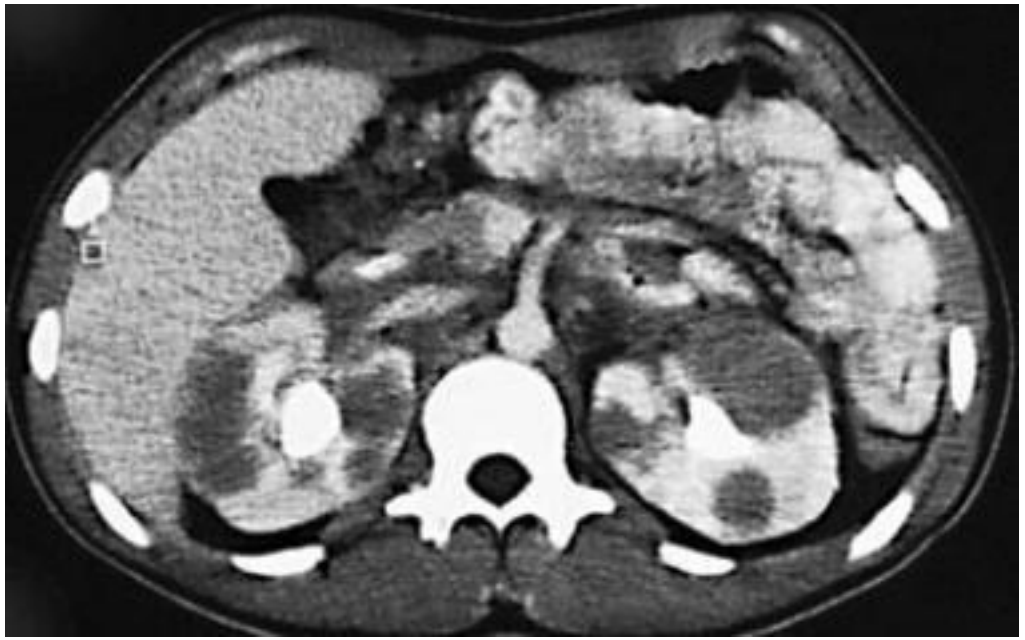
- AKI in Cancer pts is a multifactorial event

Intrinsic Causes of AKI

- unique/more frequent causes in CA pts:
- Lymphomatous Infiltration of the Kidney
- Cast Nephropathy
- Tumor Lysis Syndrome

Lymphomatous Infiltration of the Kidney (LIK)





Common but under-Dx complication of hematologic malignancies

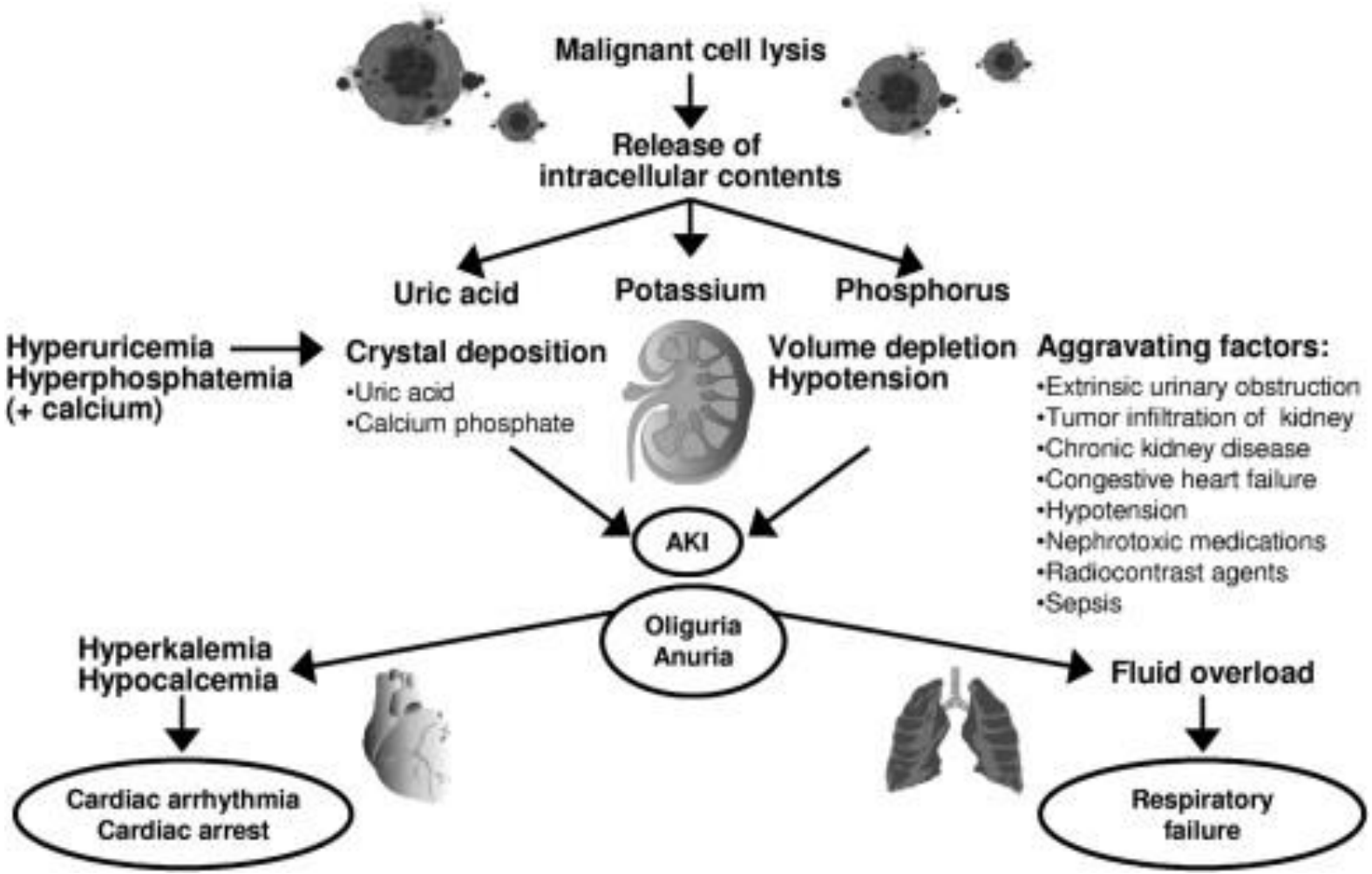
Tumor Lysis Syndrome

TLS is a medical emergency and a common cause of cancer-induced AKI

Risk Factors for TLS

- highly chem-osensitive malignancies such as lymphomas and leukemias,
- large tumor burden,
- effective cytolytic chemotherapeutic agents,
- elevated lactate dehydrogenase levels (> 1,500 IU), and
- underlying kidney disease

“any tumor”


Malignant cell lysis
Release of intracellular contents
Uric acid
Potassium
Phosphorus
Hyperuricemia
Hyperphosphatemia
(+ calcium)
Crystal deposition
•Uric acid
•Calcium phosphate
Volume depletion
Hypotension
Aggravating factors:
•Extrinsic urinary obstruction
•Tumor infiltration of kidney
•Chronic kidney disease
•Congestive heart failure
•Hypotension
•Nephrotoxic medications
•Radiocontrast agents
•Sepsis
AKI
Oliguria
Anuria
Hyperkalemia
Hypocalcemia
Cardiac arrhythmia
Cardiac arrest
Fluid overload
Respiratory failure

TLS Burden

- The **in-hospital mortality** associated with TLS can approach **21%**, and nearly 70% of patients experience a severe complication such as:
- sepsis,
- dialysis,
- acute respiratory failure,
- mechanical ventilation,
- cardiac arrest, or
- seizures

"the Cairo-Bishop definition"

- While there are **no universally accepted diagnostic criteria** for TLS, the Cairo-Bishop definition of **both laboratory and (+) clinical criteria** are commonly utilized [93].
- **Laboratory criteria** include the following:

  1- hyperuricemia (> 8 mg/dL or a 25% increase from base- line),

  2- hyperkalemia (> 6 mmol/L or 25% increase from baseline),

  3- hyperphosphatemia (> 4.5 mg/dL or 25% in- crease from baseline) and

  4- hypocalcemia (< 7 mg/dL or a 25% decrease from baseline).
- Laboratory criteria for TLS require the presence of **2 or more** of these abnormalities occurring 3 days before or 7 days after therapy.
- **Clinical criteria include**:

  1- serum creatinine elevation > 1.5 times the upper limit of normal,

  2- cardiac arrhythmias,

  3- sudden death, and

  4-seizures

Laboratory & Clinical TLS
“Cairo & Bishop”

Laboratory TLS	Clinical TLS
(Requires ≥2 laboratory abnormalities)	(Requires laboratory TLS features plus any clinical finding below)
Hyperuricemia (uric acid ≥8 mg/dl)	AKI≥
Hyperphosphatemia (>4.5 mg/dl in adults; >6.5 mg/dl in children)	Stage I (AKIN criteria)≥ R (RIFLE criteria)
Hyperkalemia (potassium >6.0 mEq/L)	Cardiac dysrhythmia, sudden death
Hypocalcemia (corrected serum calcium <7.0 mg/dl, or ionized calcium <1.12 mg/dl)	Cardiac dysrhythmia, sudden death, seizure, tetany, carpopedal spasm, bronchospasm, laryngospasm, hypotension

Clinical TLS

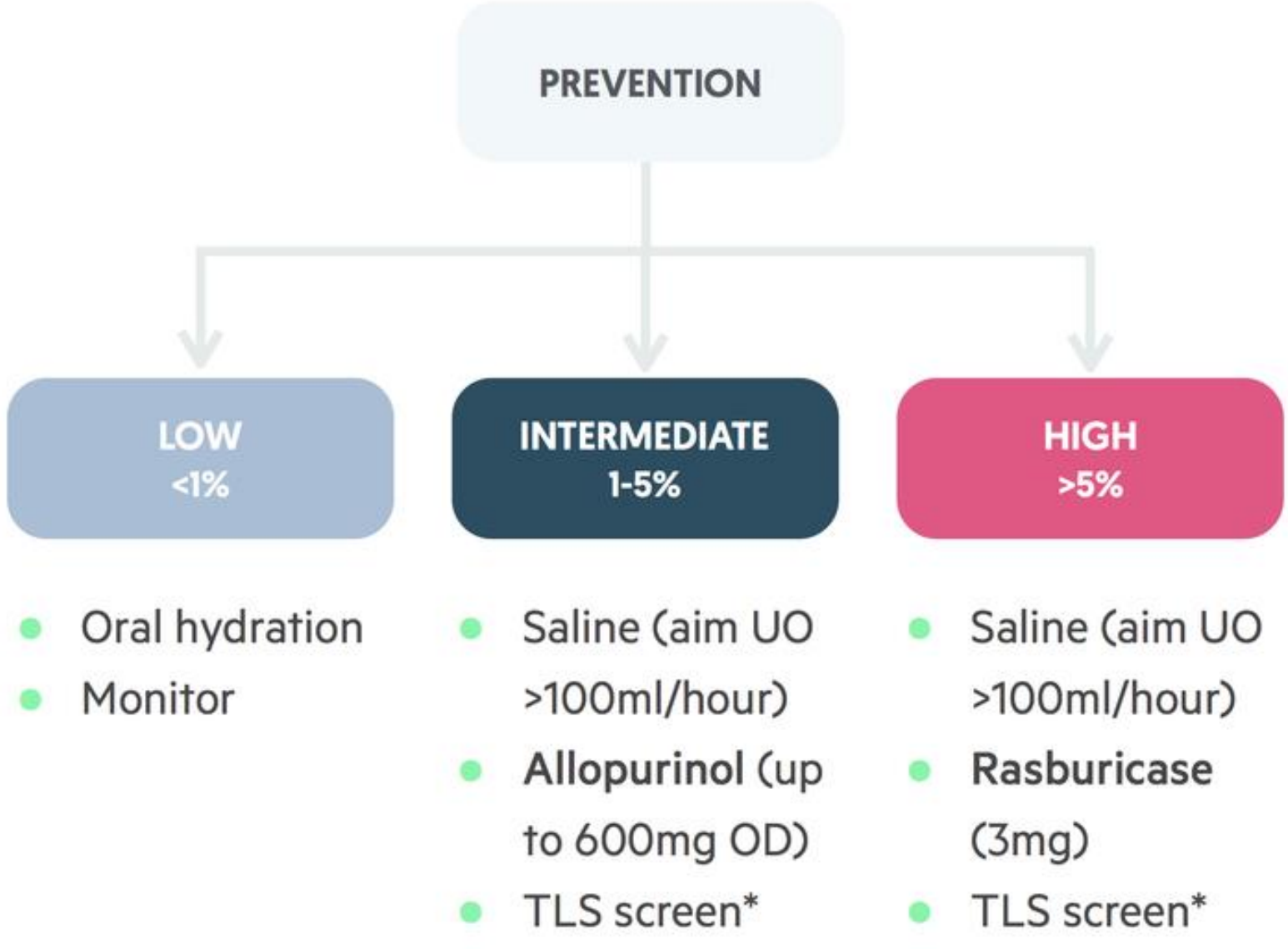
	0	1	2	3	4	5
Creatinine	< 1.5x	1.5 - 3 x	1.5 - 3 x	3 - 6 x	> 6 x	Death
Arrthymias	No	Intervention not indicated	Intervention indicated	Symptomatic, urgent action.	Life-threatening	Death
Seizures	No	-	Single, easily controlled	Repeated, altered consciousness	Prolonged, refractory	Death

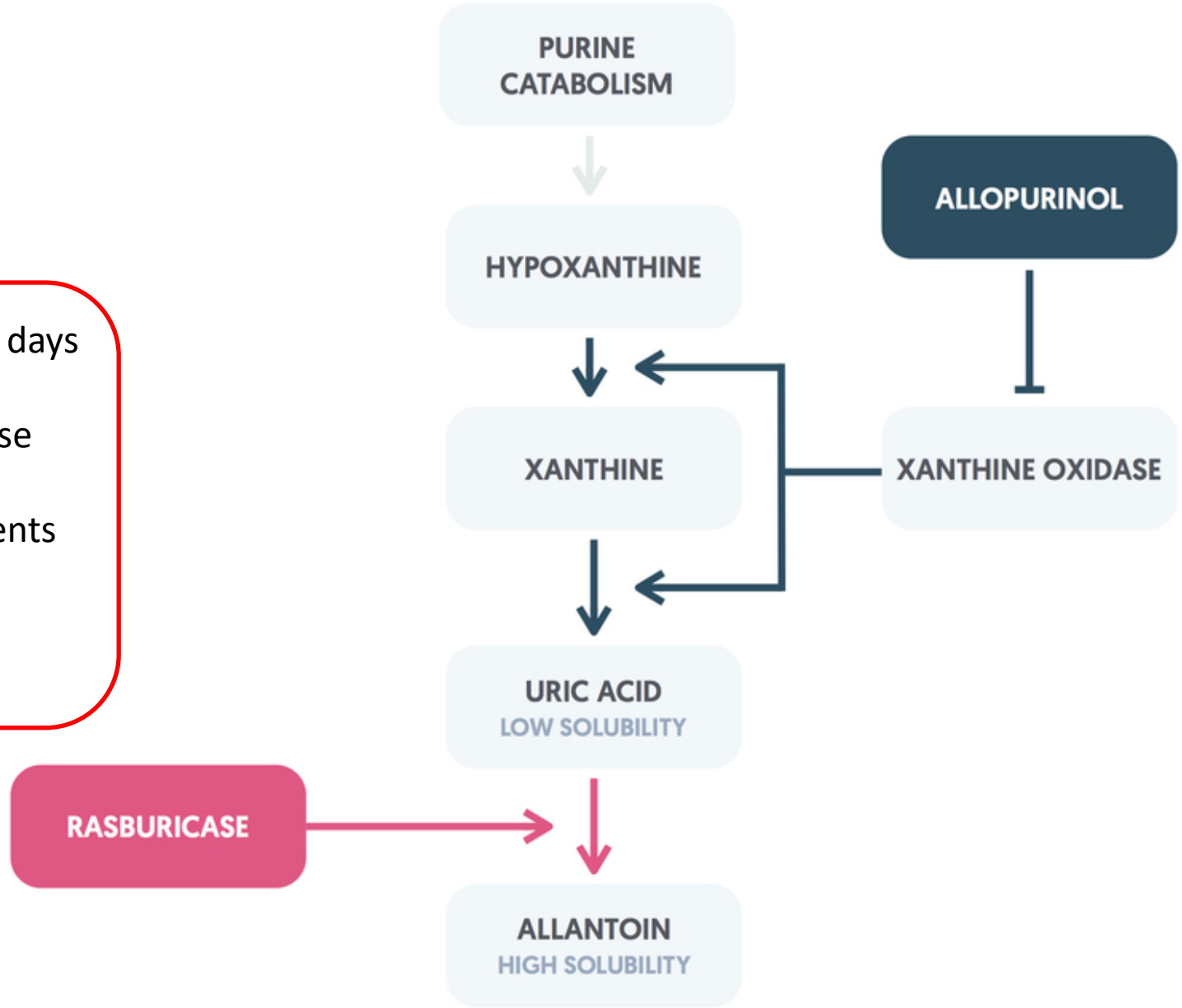
Cairo-Bishop: Clinical grading of tumour lysis syndrome.

Variable	Grade 0	Grade I	Grade II	Grade III	Grade IV	Grade V
Creatinine	None	1.5 times upper limits of normal (ULN)	>1.5-3.0 times ULN	>3.0-6.0 times ULN	>6.0 times ULN	Death
Cardiac arrhythmia	None	Intervention not indicated	Nonurgent medical intervention indicated	Symptomatic and incompletely controlled medically or controlled with device (e.g., defibrillator)	Life-threatening (e.g., arrhythmia associated with HF, hypotension, syncope, shock)	Death
Seizures	None	–	One brief, generalized seizure; seizure(s) well controlled by anticonvulsants or infrequent focal motor seizures not interfering with ADL	Seizure in which consciousness is altered; poorly controlled seizure disorder; with breakthrough generalized seizures despite medical intervention	Seizure of any kind which are prolonged, repetitive or difficult to control (e.g., status epilepticus, intractable epilepsy)	Death

Prophylaxis against TLS
is recommended for all patients
with hematological malignancies
undergoing chemotherapy

Prophylaxis is also recommended for
all high and moderate risk patients
such as those with large tumor burdens,
reduced GFR, and
highly chemosensitive tumors


PREVENTION
LOW
<1%
INTERMEDIATE
1-5%
HIGH
>5%
Oral hydration
Monitor
Saline (aim UO >100ml/hour)
Allopurinol (up to 600mg OD)
TLS screen*
Saline (aim UO >100ml/hour)
Rasburicase (3mg)
TLS screen*



0.2 mg/kg for 3-5 days
Or
6 mg single dose

Few adverse events (met-Hgb)

Cost ?

600 mg IV or 800 mg PO

-d2 untill +d3

Multiple interaction/dose adjust/avoidance

No effect on “already” uric acid

Xanthine precipitation

- **Febuxostat** is a non-purine analogue **xanthine oxidase inhibitor** and is useful in patients that are intolerant to allopurinol.

- Trials demonstrated that febuxostat was superior in lowering uric acid levels but there was *no difference* in clinical outcomes *vs. allopurinol*

- Febuxostat dosing should be **40 mg daily** in patients with severe kidney function impairment.

Randomized trials of Rasburicase

Study	Year	Patients (*n*)	Population	Group 1	Group 2	End Point
Cortes *et al.* (61)[a]	2010	183	Adults at risk for TLS	Rasburicase, 0.20 mg/kg per d for 5 d	Allopurinol, 300 mg/d for 5 d	Uric acid <7.5 mg/dl at 3–7 d
Malaguarnera *et al.* (68)	2009	38	Hyperuricemic elderly patients	Rasburicase, 4.5 mg for 1 dose	Placebo	Change in uric acid at 1 wk
Kikuchi *et al.* (92)	2009	30	Japanese children at risk for TLS	Rasburicase, 0.20 mg/kg per d for 5 d	Rasburicase, 0.15 mg/kg per d for 5 d	Sustained reduction in uric acid to <6.5 mg/dl (age <13 yr) or <7.5 mg/dl (age ≥13 yr)
Ishizawa *et al.* (93)	2009	50	Japanese adults at risk for TLS	Rasburicase, 0.20 mg/kg per d for 5 d	Rasburicase, 0.15 mg/kg per d for 5 d	Sustained reduction of uric acid <7.5 mg/dl
Goldman *et al.* (77)	2001	52	Children at risk for TLS	Rasburicase, 0.20 mg/kg per d for 5–7 d	Allopurinol, 300 mg every 8 h for 5–7 d	Area under the uric acid curve over 5 d

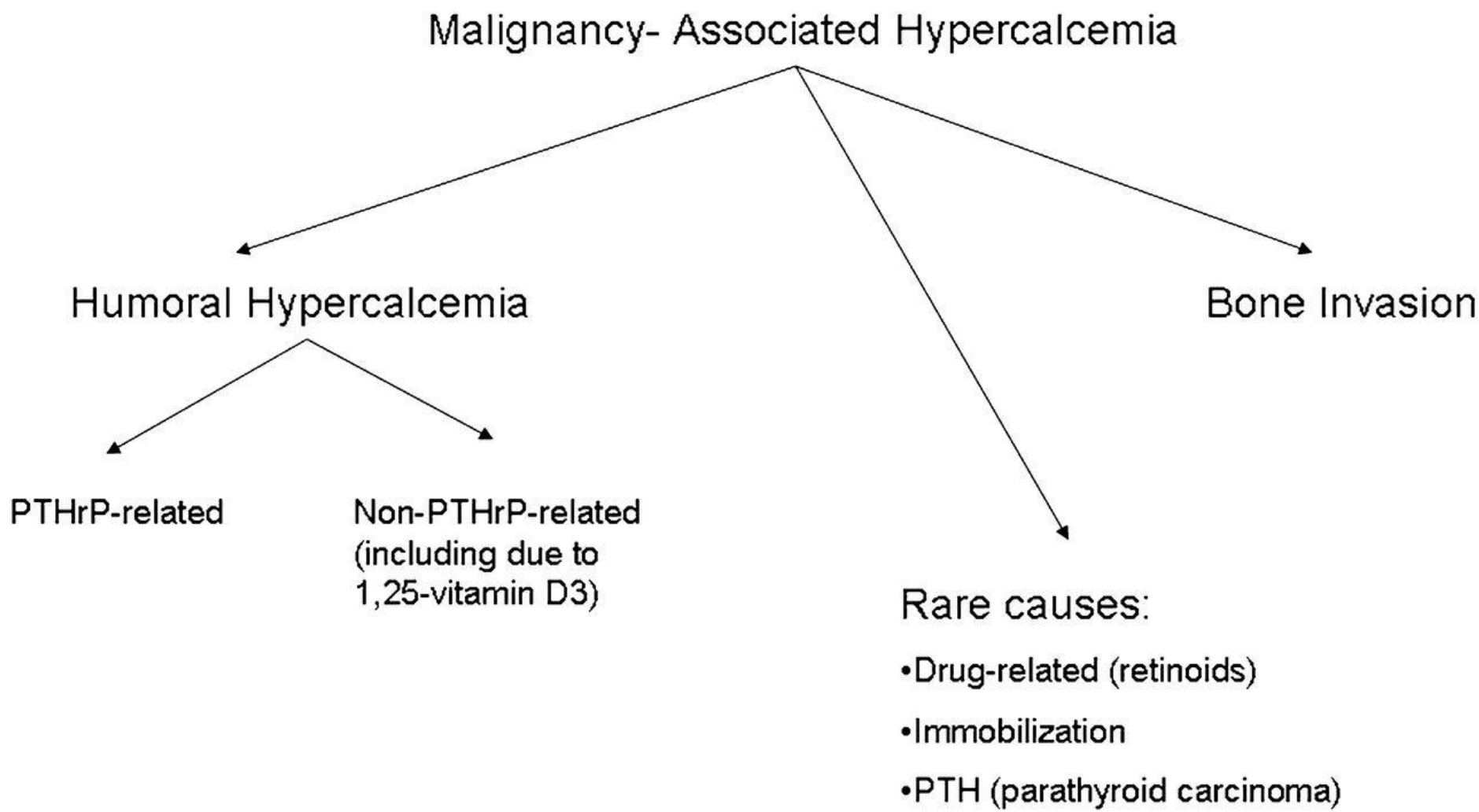
Wilson and Berns CJASN 2012

The need for hemodialysis to treat TLS
has likely declined
since the advent of ***rasburicase***

RRT & TLS

- Hemodialysis remains a highly effective therapy that can be used to gain control of electrolyte and acid-base issues, especially in the presence of oliguric AKI.
- **Continuous renal replacement therapies** can be utilized in the treatment of TLS and have the advantage of avoiding "rebound" metabolic disturbances.
- If a continuous renal replacement is utilized, **higher clearance levels** (at least **30-40** mL/kg/ hour) should be targeted.

Hypercalcemia- Induced AKI


Malignancy- Associated Hypercalcemia
Humoral Hypercalcemia
Bone Invasion
PTHrP-related
Non-PTHrP-related
(including due to
1,25-vitamin D3)
Rare causes:
•Drug-related (retinoids)
•Immobilization
•PTH (parathyroid carcinoma)

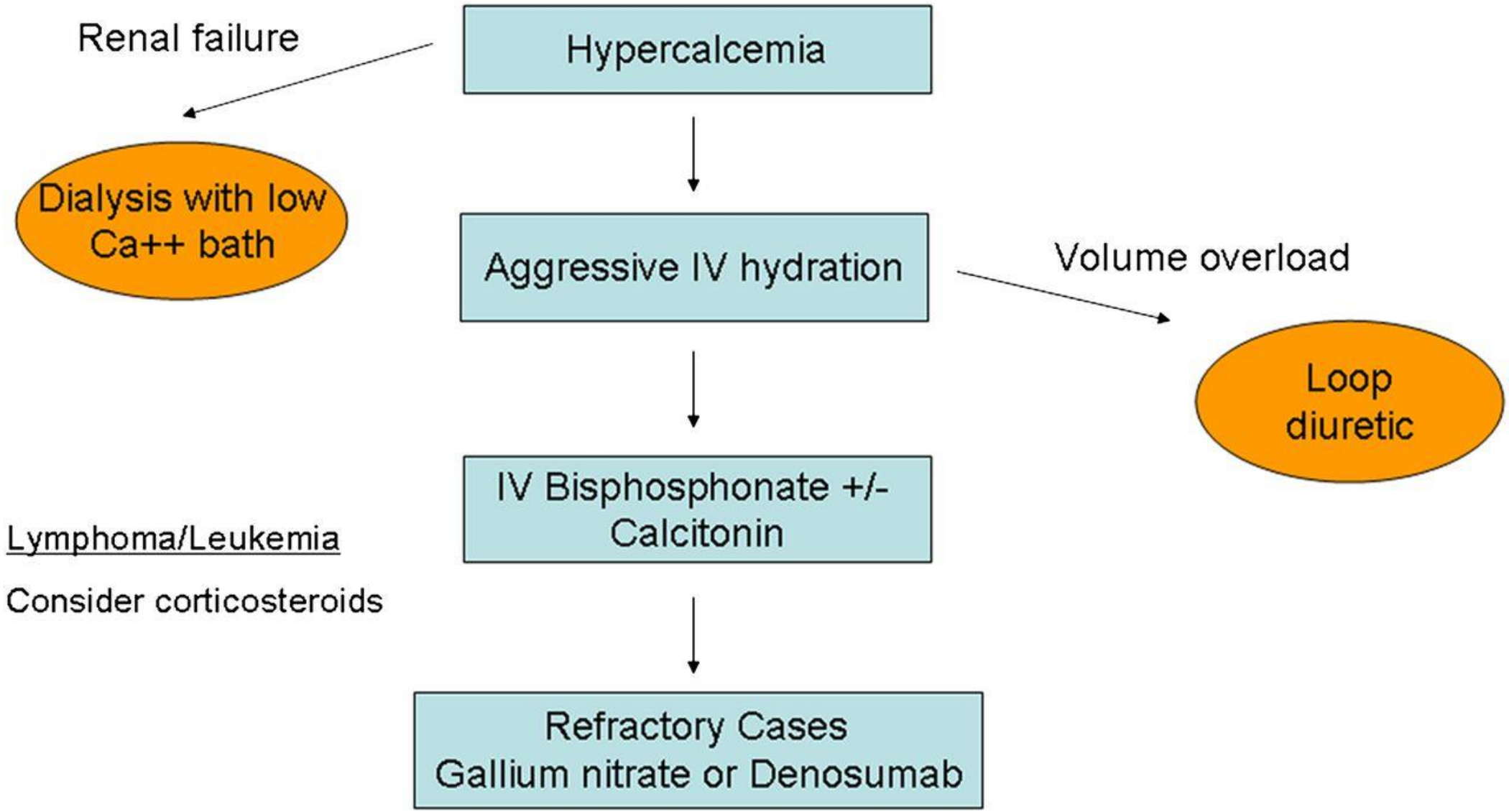
- Hypercalcemia occurs in approximately **20% to 30%** of all malignancies (especially, **multiple myeloma** and **squamous cell carcinomas**) and is a common cause of AKI
- In some scenarios, such as with multiple myeloma, the presence of hypercalcemia may potentiate other AKI etiologies
- Hypercalcemia promotes direct afferent arteriolar vasoconstriction and also leads to volume depletion from excessive renal sodium and water loss

Table 1. Types of Hypercalcemia Associated with Cancer.*

Type	Frequency (%)	Bone Metastases	Causal Agent	Typical Tumors
Local osteolytic hypercalcemia	20	Common, extensive	Cytokines, chemokines, PTHrP	Breast cancer, multiple myeloma, lymphoma
Humoral hypercalcemia of malignancy	80	Minimal or absent	PTHrP	Squamous-cell cancer, (e.g., of head and neck, esophagus, cervix, or lung), renal cancer, ovarian cancer, endometrial cancer, HTLV-associated lymphoma, breast cancer
$1,25(OH)_2D$-secreting lymphomas	<1	Variable	$1,25(OH)_2D$	Lymphoma (all types)
Ectopic hyperparathyroidism	<1	Variable	PTH	Variable

- Hypercalcemia causes sodium wasting at the loop of Henle by activating the calcium-sensing receptor,
- and also leads to **renal water losses** by **blocking arginine vasopressin activity in the distal nephrons**

- Rosner MH, Perazella MA. Acute kidney injury in patients with cancer. N Engl J Med 2017;376:1770-1781.


Renal failure
Hypercalcemia
Dialysis with low Ca++ bath
Aggressive IV hydration
Volume overload
Loop diuretic
IV Bisphosphonate +/- Calcitonin
Lymphoma/Leukemia
Consider corticosteroids
Refractory Cases
Gallium nitrate or Denosumab

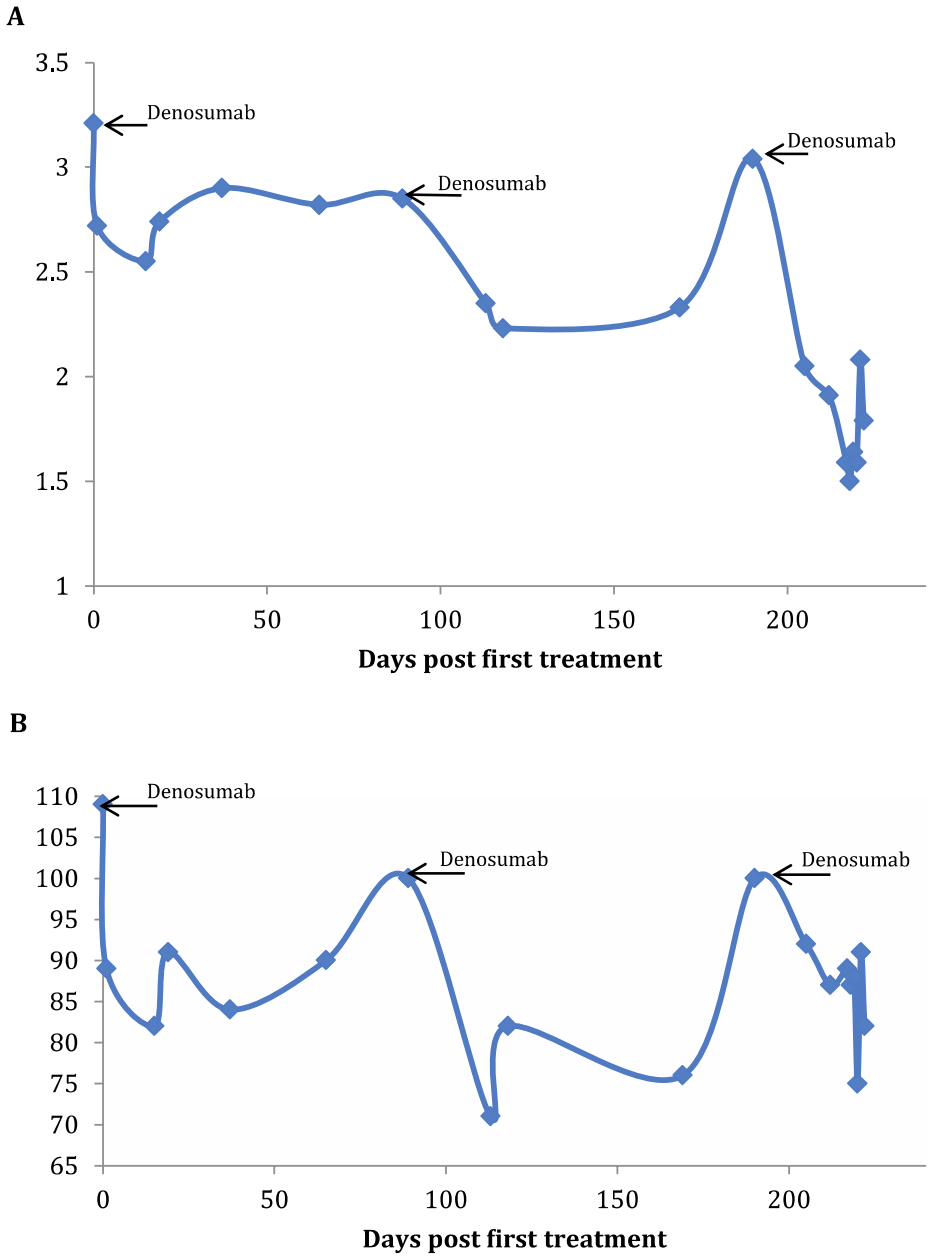
DENOSUMAB

THIS HUMAN MONOCLONALANTIBODY IS EFFECTIVE IN THE TREATMENT OF HYPERCALCEMIA OF MALIGNANCY.

CORRESPONDENCE

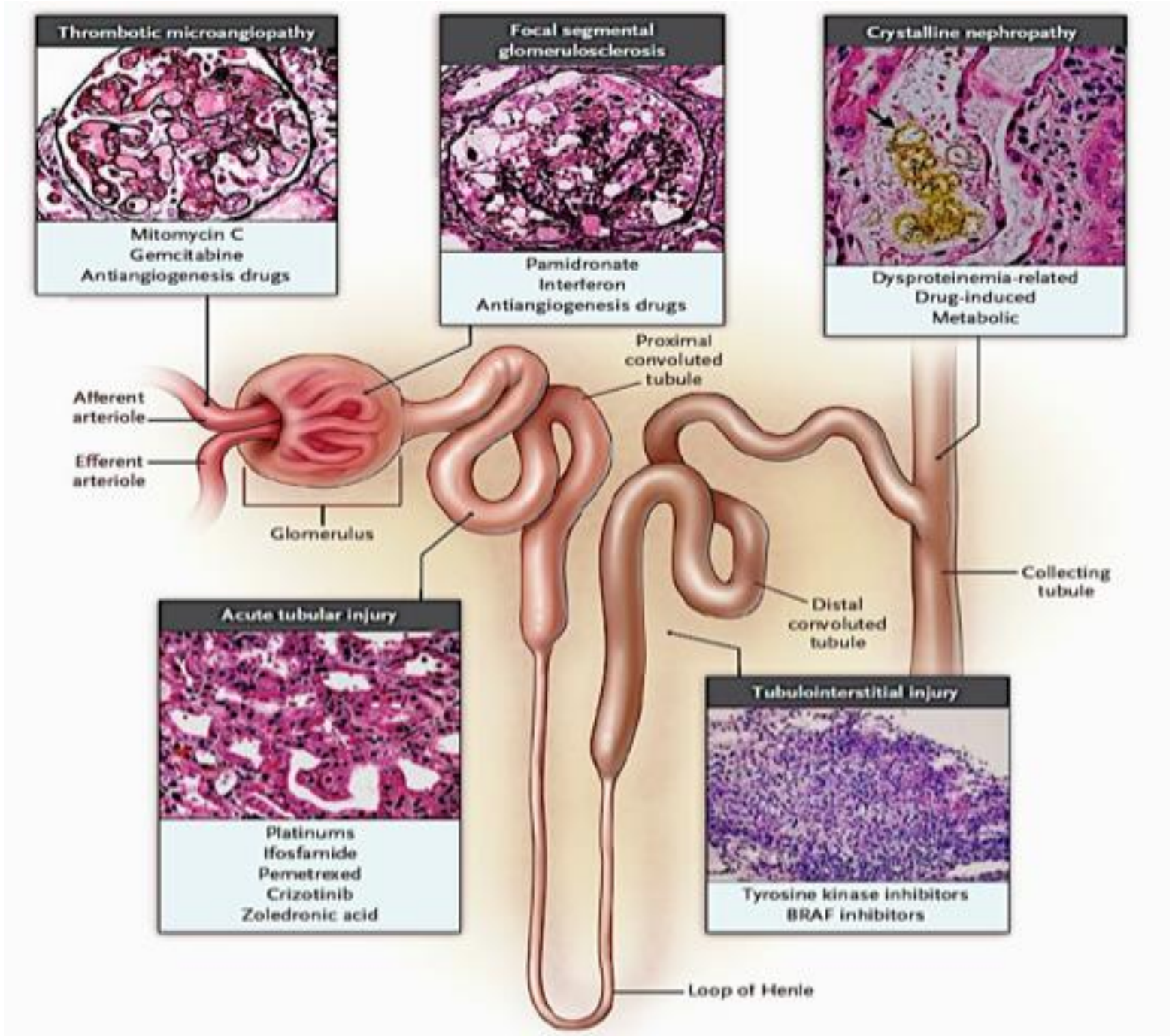
RE: Denosumab for Patients With Persistent or Relapsed Hypercalcemia of Malignancy Despite Recent Bisphosphonate Treatment

Jason Adhikaree, Yvette Newby, Santhanam Sundar



. **A)** Adjusted Calcium mmol/L post–denosumab treatment. **B)** Creatinine umol/L post–denosumab treatment.

Drug-Induced AKI


Thrombotic microangiopathy
Mitomycin C
Gemcitabine
Antiangiogenesis drugs
Focal segmental glomerulosclerosis
Pamidronate
Interferon
Antiangiogenesis drugs
Crystalline nephropathy
Dysproteinemia-related
Drug-induced
Metabolic
Proximal convoluted tubule
Afferent arteriole
Efferent arteriole
Glomerulus
Collecting tubule
Distal convoluted tubule
Acute tubular injury
Platinums
Ifosfamide
Pemetrexed
Crizotinib
Zoledronic acid
Tubulointerstitial injury
Tyrosine kinase inhibitors
BRAF inhibitors
Loop of Henle

- chemotherapy-associated AKI can be separated into 3 drug classes:

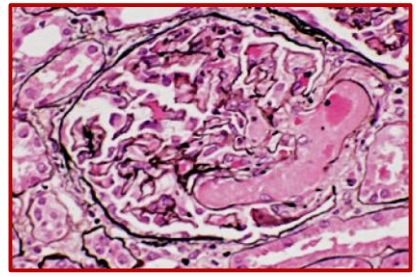
  1) conventional chemotherapy,

  2) targeted therapies, and

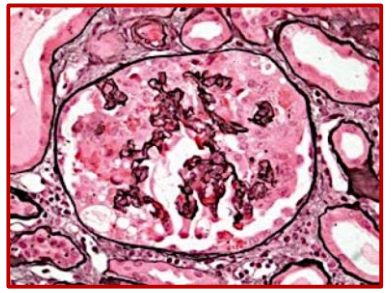
  3) novel immunotherapies

Conven2onal Chemotherapeu2c Agents

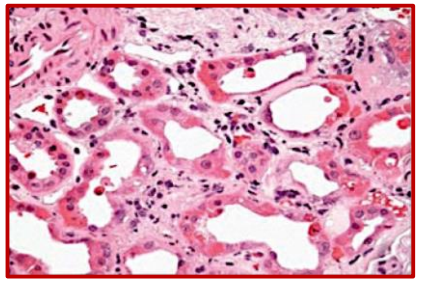
- Gemcitabine, Mitcomycin C, Cispla2n – TMA



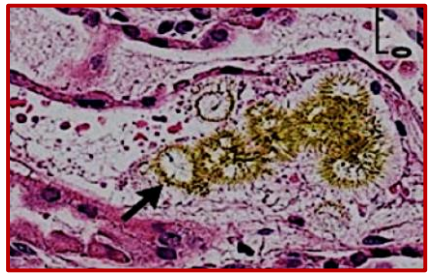
- Pamidronate – Collapsing FSGS



- Pla2ns, Ifosfamide, Pemetrexed, Zoledronate – Toxic ATI/ATN



- Methotrexate – Crystalline ATI



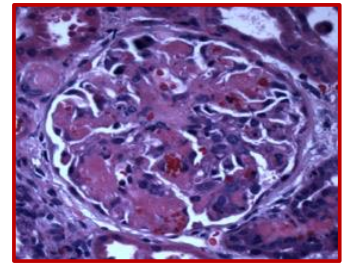
Target Agents

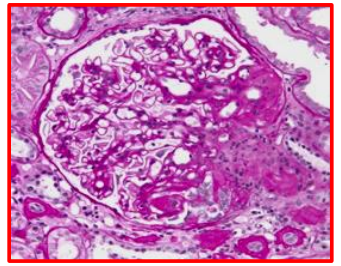
very successful in effectively treating cancer,
but unfortunately are also associated with
AKI, proteinuria, hypertension, and electrolyte disturbances

Targeted An2-Cancer Agents

- An2-VEGF Inhibitors—

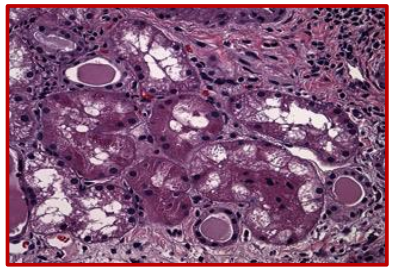
TMA, MCD/FSGS





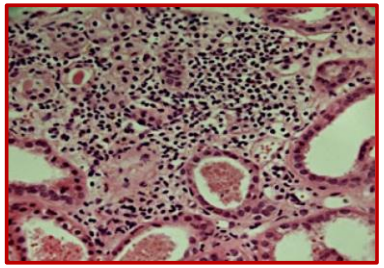
- ALK Inhibitors—

AKI, Renal Cyst



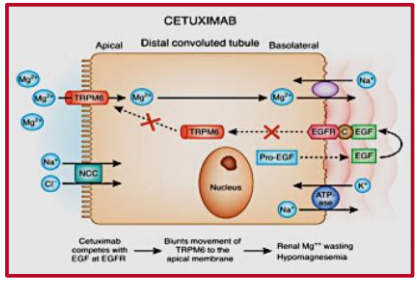
- BRAF Inhibitors—

AIN/ATN



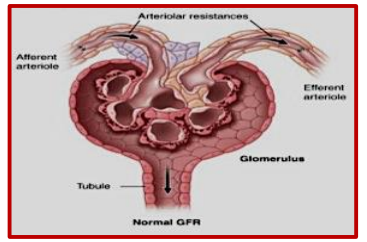
- EGFR an2 bodies—

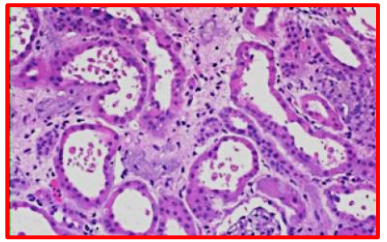
Hypomagnesemia



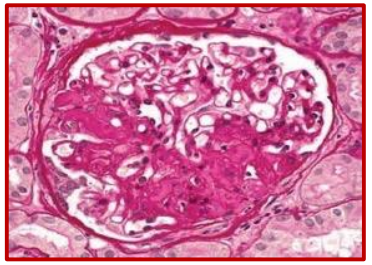
Cancer Immunotherapies

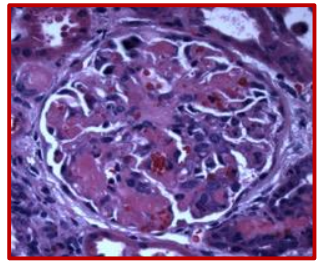
- **Interleukin-2–** Prerenal AKI, ATN, PI-GN



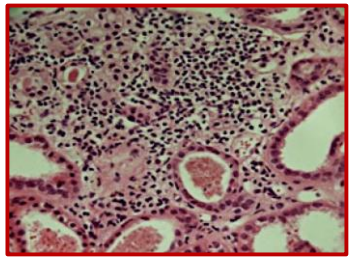


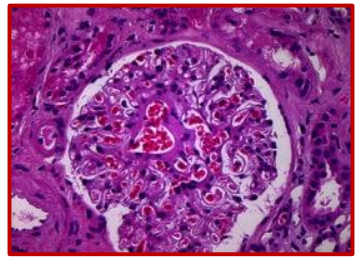
- **Interferon–** FSGS / TMA



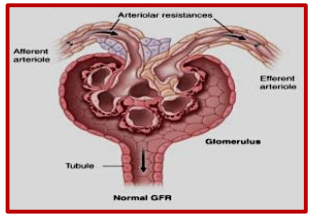


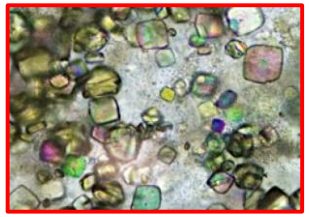
- **Immune Checkpoint Inhibitors–** AIN/IC-GN/MCD Txp rejection



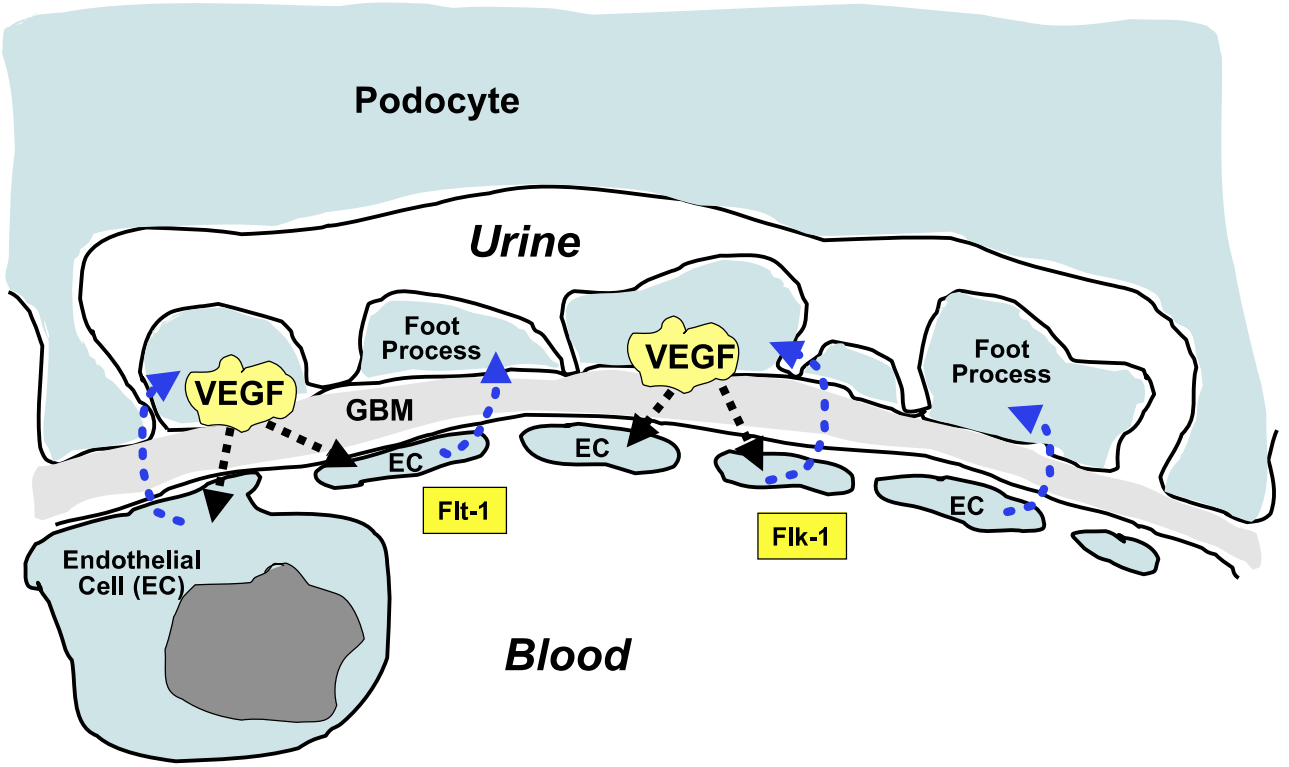


- **CAR T-Cells–** Prerenal AKI/ATI, TLS, electrolyte disorders

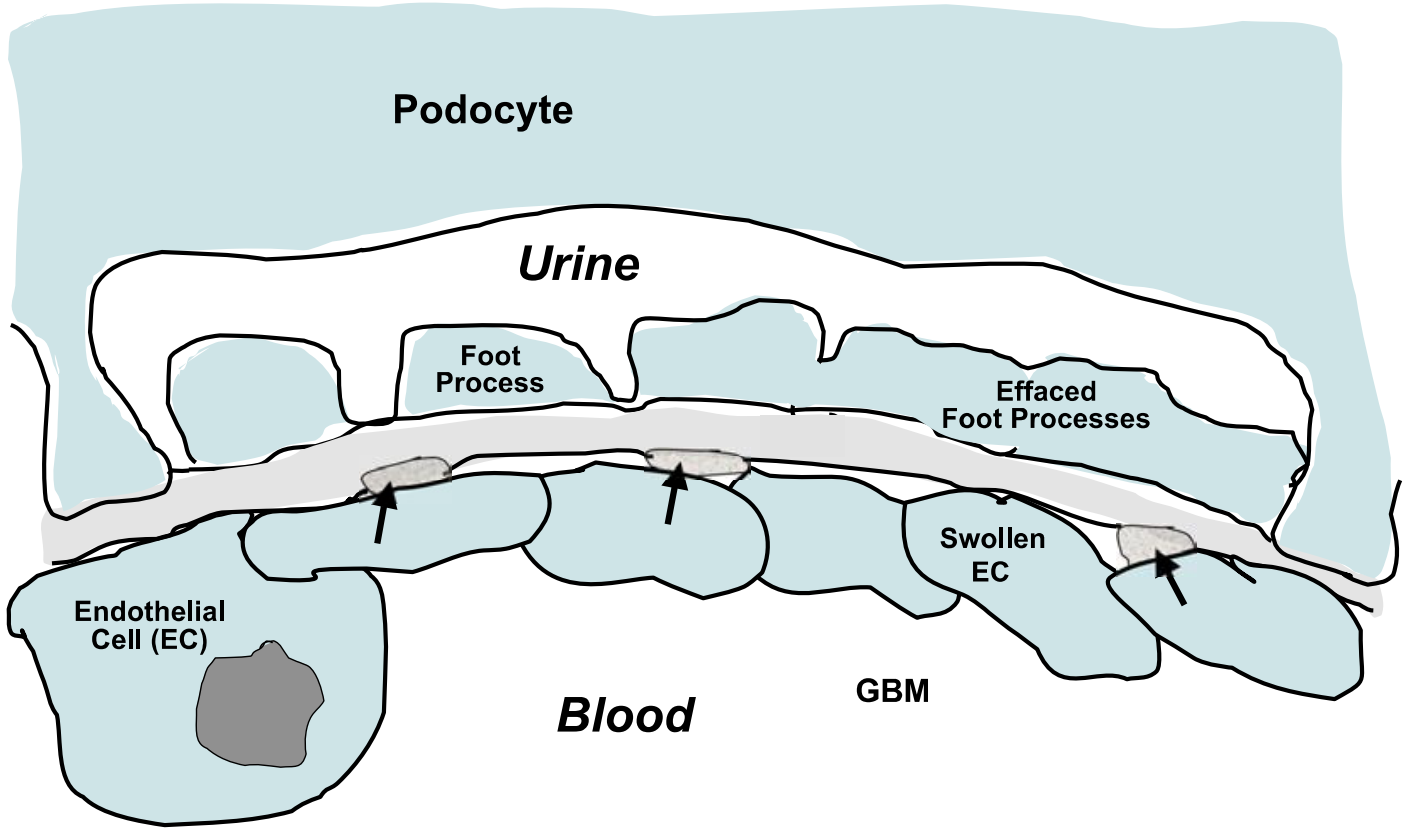




VEGF & Proteinuria



VEGF & Proteinuria



AKI after HCT

Table 1. Selected studies from the last decade in critically ill patients with HM and AKI

References	Patients with HM	Design and setting	BMT / HSCT	RRT	Survival	Main findings
Lengline *et al.* 2015 [24]	123	Retrospective, multicenter	Allogenic, 100%	57 (46%)	Hospital, 52% 3 months, 49%	The use of RRT was independently associated with 90-day mortality. 95% of the patients managed with RRT died after a median <2 weeks.
Canet *et al.* 2014 [9]	49	Retrospective, single center	Allogenic, 100%	3 (6%)	Hospital, 53% 3 months, 35%	Mortality was associated with the severity of AKI, GVHD and VOD. No surviving patients recovered previous renal function at 3-months of follow-up.
Canet *et al.* 2013 [2]	137	Prospective, single center	None	72 (53%)	Hospital, 65% 6 months, 53%	AKI was associated with lower rates of complete remission. Renal recovery occurred in 92% among hospital survivors.
Azoulay *et al.* 2013 [25]	204 (out of 1032 patients with HM)	Prospective, multicenter	252 (25%) (allogenic = 145; autologous =107)	262 (26%)	Hospital, 59%	Patients treated with RRT had a hospital mortality of 59%, but among those without any other organ failure than AKI, 81% were alive at hospital discharge
Park *et al.* 2011 [26]	94	Retrospective, single center	21 (22%) (allogenic = 12; autologous = 9)	100%	ICU, 23%	Nonrenal organ dysfunctions were associated with ICU mortality.
Darmon *et al.* 2007 [7]	87 (out of 94 patients with cancer)	Prospective, single center	None	100%	Hospital, 48%	The severity of associated organ failures and renal function deterioration after ICU admission were associated with worse outcomes. Mortality was comparable to noncancer patients.
Soares *et al.* 2006 [3]	76 (out of 309 patients with cancer)	Prospective, single center	None	34 (45%)	Hospital, 24% 6 months, 13%	Older age, uncontrolled cancer, impaired performance status and associated organ failures were associated with increased 6-month mortality. Renal function was completely reestablished in 82%.
Benoit *et al.* 2005 [21]	49 (out of 270 patients with cancer)	Retrospective, single center	None	42 (86%)	ICU, 20% Hospital, 16%	Hematological patients had higher rate of AKI treated with RRT and mortality than other patients. However, hematological malignancy was not independently associated with death.

AKI, acute kidney injury; BMT, bone marrow transplant; GVHD, graft versus host disease; HM, hematological malignancies; HSCT, hematopoietic stem-cell transplant; ICU, intensive care unit; VOD, veno-occlusive disease.

- The original report by Zager et al., which analyzed 272 patients undergoing **myeloablative HCT** (89% allogeneic and 11% autologous), found that 53% of patients developed AKI (defined as doubling of serum creatinine), with one-half of these patients requiring dialysis.

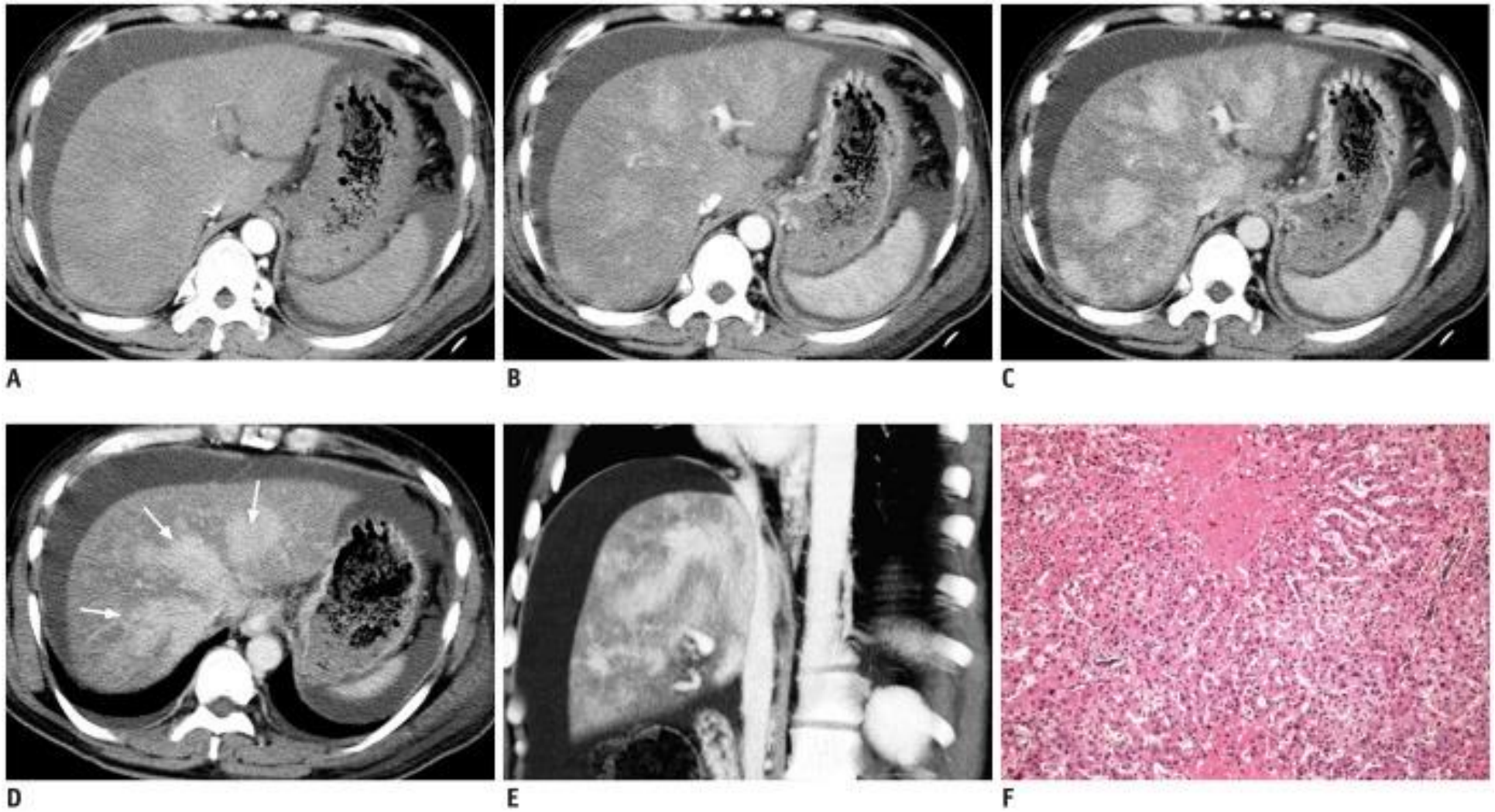
- This remarkably **high incidence of AKI in myeloablative & allogeneic HCT** has been confirmed in several more recent studies

- Overall **mortality** rates in patients with **AKI** range from **37% to 46%** and are as high as 88% in patients requiring dialysis

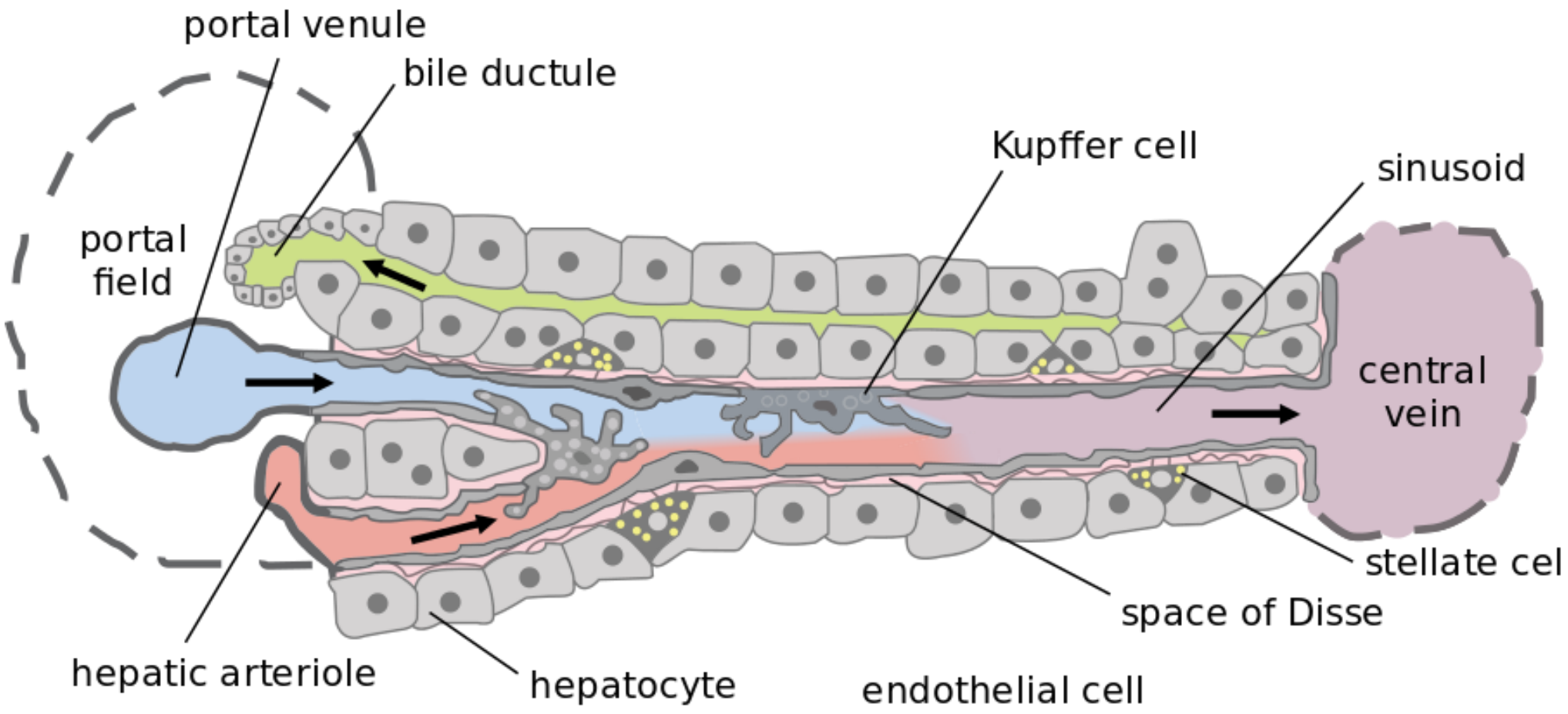
AKI after HCT

- Early onset (<30 days)
  - Sepsis
  - Hypotension
  - Hypovolemia (vomiting and diarrhea)
  - Nephrotoxic agents
    - Acyclovir
    - Allopurinol
    - Amphotericin B
    - Angiotensin-converting enzyme inhibitors
    - Angiotensin receptor blockers
    - Calcineurin inhibitors
    - Contrast dye
    - Methotrexate
    - NSAIDs
  - Tumor lysis syndrome
  - Hepatic sinusoidal obstruction syndrome
- Late onset (>3 months)
  - Thrombotic microangiopathy
  - Calcineurin inhibitor toxicity

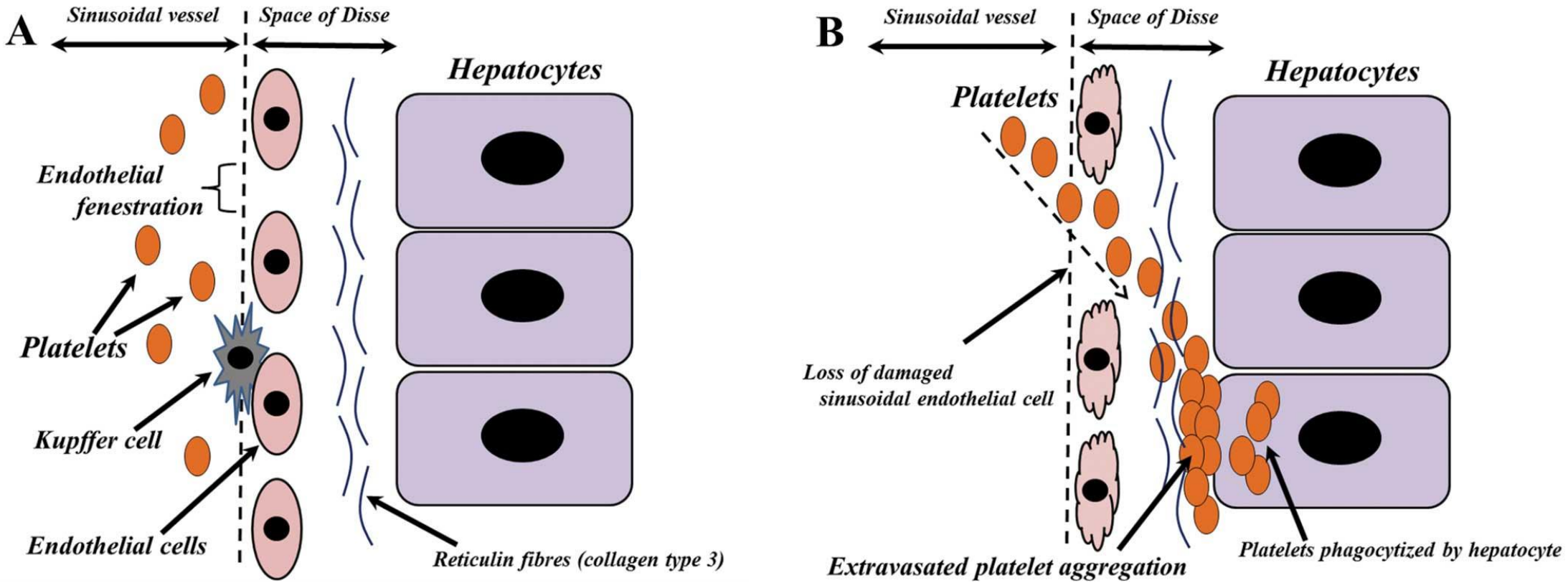
Hepatic sinusoidal obstruction syndrome (SOS)



Hepatic sinusoidal obstruction syndrome (SOS)



Hepatic sinusoidal obstruction syndrome (SOS)



Hepatic sinusoidal obstruction syndrome (SOS)

- **Hepatic sinusoidal obstruction syndrome** (SOS), previously known as veno-occlusive disease, is the constellation of:

  1- tender hepatomegaly,

  2- fluid retention,

  3- weight gain, and

  4- jaundice

- that occurs after the administration of high-dose conditioning regimens, including **cyclophosphamide**, busulfan, and/or **total body irradiation**

- Although SOS has historically been reported in 5%–60% of patients, a recent review of studies performed between 1979 and 2007 found that the overall mean **incidence** of SOS was **13.7%**

- SOS occurs more commonly after **myeloablative allogeneic** HCT than after autologous HCT ,
- and it is essentially **nonexistent with nonmyeloablative** regimens.
- **Risk factors** for developing SOS include:

1- older age,

2- pre-existing liver disease,

3- medications (methotrexate, itraconazole, sirolimus, and norethisterone), and

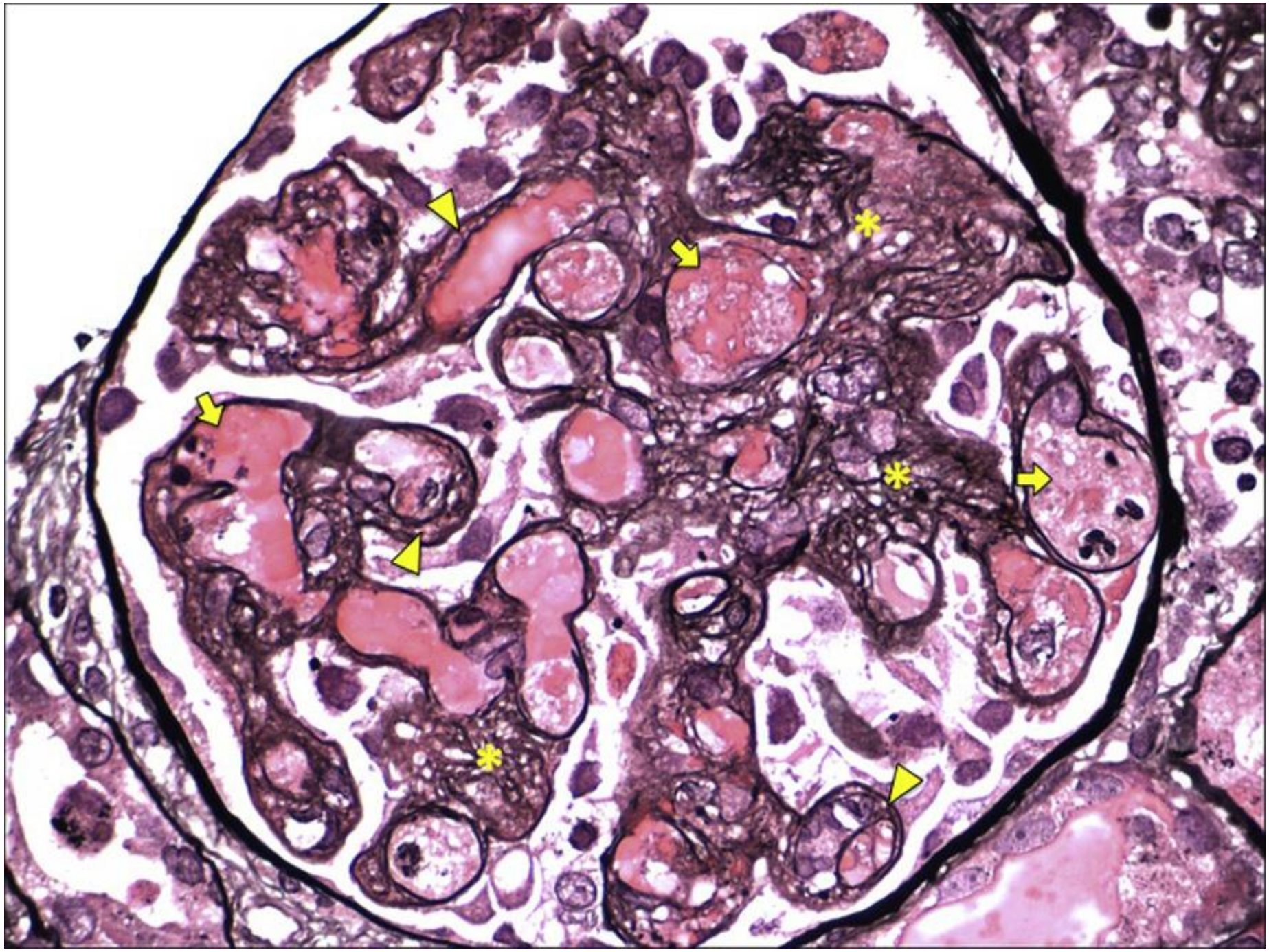
4- certain conditioning agents (cyclophosphamide and busulfan)

AKI develops in approximately 50% of patients with SOS

and is clinically indistinguishable from the hepatorenal syndrome

Rx of SOS

- More than 70% patients with SOS will recover spontaneously with only supportive therapy, which consists of maintaining sodium and water balance, preserving renal blood flow, and treating symptomatic ascites with repeated paracenteses.
- For patients with **severe SOS**, there are **no highly effective treatments**, although the best results have been achieved with defibrotide, a single-stranded oligodeoxyribonucleotide with antithrombotic and profibrinolytic properties that has a 46% complete response rate.
- Infusion of heparin and/or ursodeoxycholic acid administered immediately **before induction** therapy may also be moderately successful **as preventive measures.**



TMA

Previously known as

“bone marrow transplant nephropathy” or

“radiation nephropathy”

Thrombotic Microangiopathy

- Thrombotic microangiopathy (TMA) is a common cause of late-onset AKI in patients who have undergone HCT.
-
- TMA in cancer patients can be classified as:

  1- cancer-related TMA,

  2- cancer drugs-induced TMA (types I and II), and

  3-HSCT-related TMA

TMA is a potentially severe kidney lesion
with untoward outcomes
that can complicate certain malignancies
and a number of cancer therapies

- Cancer-related TMA mainly occurs in patients with
- **solid tumors**, most commonly in **adenocarcinomas**.

- Thrombocytopenia with micro-angiopathic hemolytic anemia and no alternative diagnosis
is sufficient to establish a presumptive diagnosis of TMA

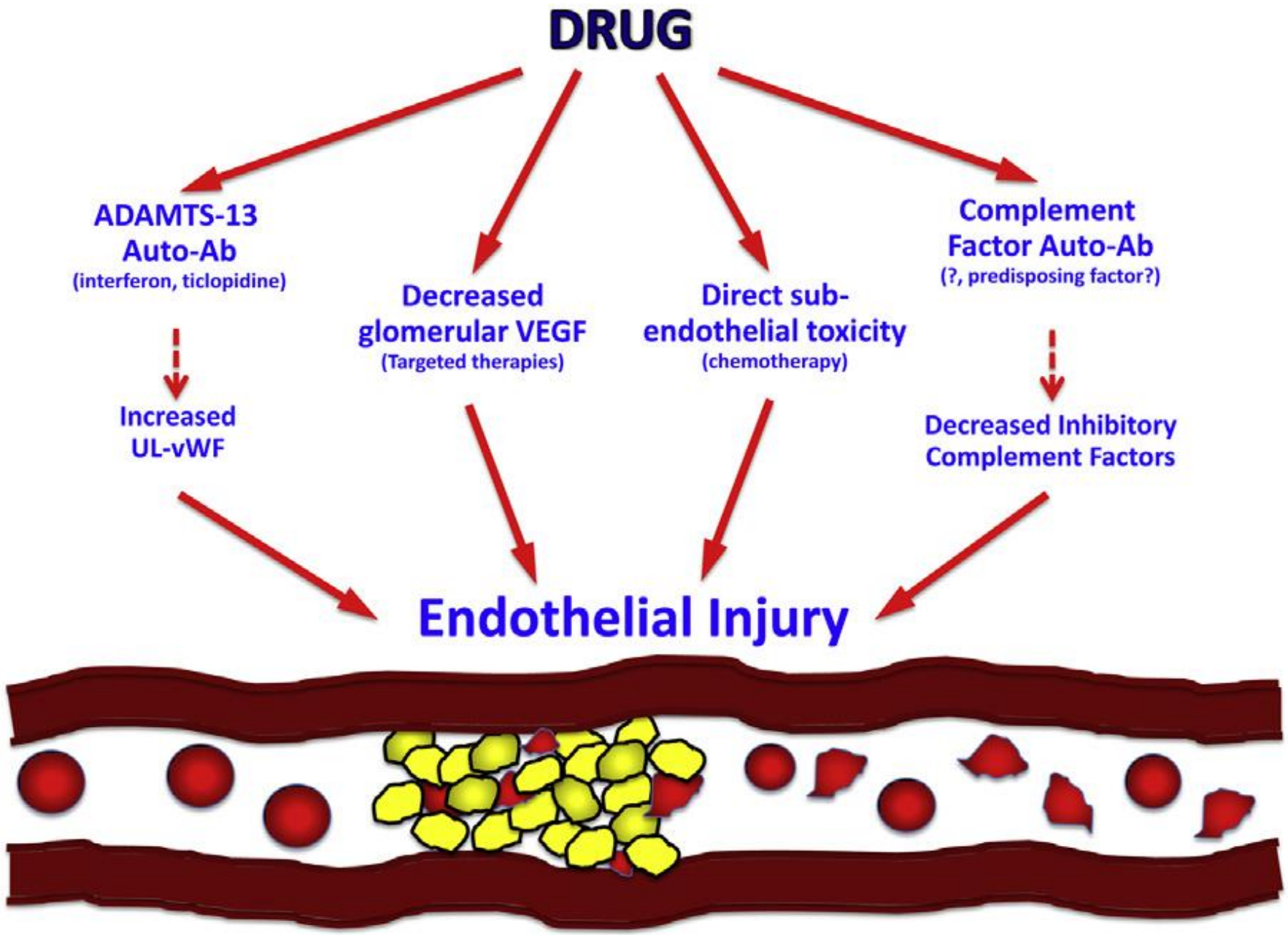
- The pathogenesis of TMA after HCT is not well understood, but damage to renal endothelial cells likely plays a central role
- The **conditioning regimen**, particularly the use of **total body irradiation**, is a primary cause of renal endothelial damage, with post-HCT factors such as **GVHD**, **infections**, and **medications** (such as the **calcineurin inhibitors**) playing a later modulatory role
- Strategies such as partial **shielding of the kidneys**, hyperfractionation of the radiation dose, and **slow radiation** administration have been proposed to reduce radiation injury.
- these approaches run the risk of decreasing the effectiveness of tumor cell eradication.

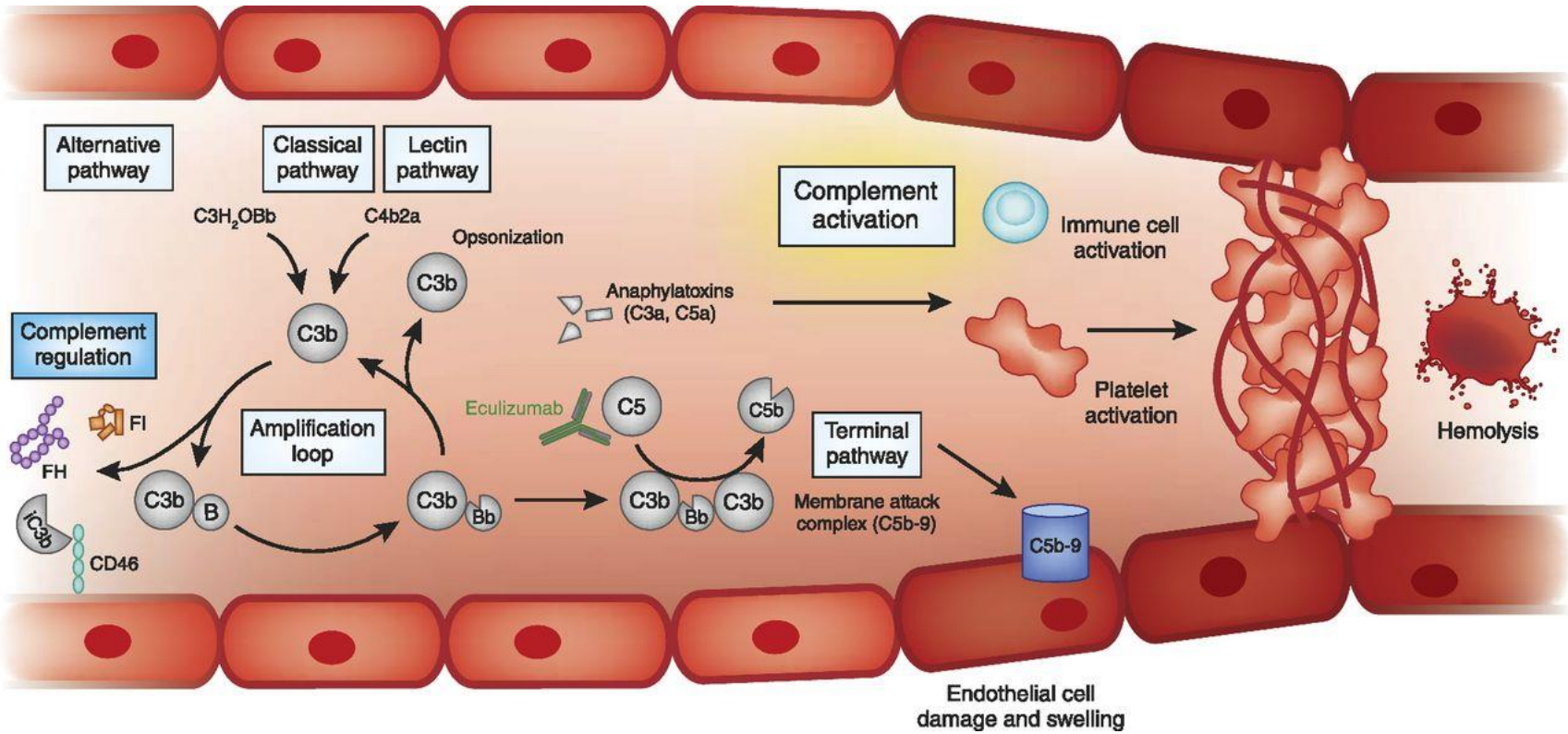
Rx of HCT- associated TMA

- The **management** of HCT- associated TMA is otherwise largely supportive.
- Calcineurin inhibitors are typically discontinued,
- Other oral agents that can be used for the prevention and treatment of GVHD include **mycophenolate mofetil and corticosteroids**.
- Substitution of calcineurin inhibitors with **daclizumab**,
- Rituximab

the incidence of **drug-induced** TMA is >15%,

primarily due to the introduction **of VEGF agents**.


DRUG
ADAMTS-13
Auto-Ab
(interferon, ticlopidine)
Decreased
glomerular VEGF
(Targeted therapies)
Direct sub-
endothelial toxicity
(chemotherapy)
Complement
Factor Auto-Ab
(?, predisposing factor?)
Increased
UL-vWF
Decreased Inhibitory
Complement Factors
Endothelial Injury


Alternative pathway
Classical pathway
Lectin pathway
C3H2OBb
C4b2a
Opsonization
C3b
Complement regulation
Amplification loop
FH
FI
iC3b
CD46
C3b
B
C3b
Bb
Eculizumab
C5
C5b
C3b
Bb
C3b
Anaphylatoxins (C3a, C5a)
Complement activation
Immune cell activation
Platelet activation
Terminal pathway
Membrane attack complex (C5b-9)
C5b-9
Hemolysis
Endothelial cell damage and swelling

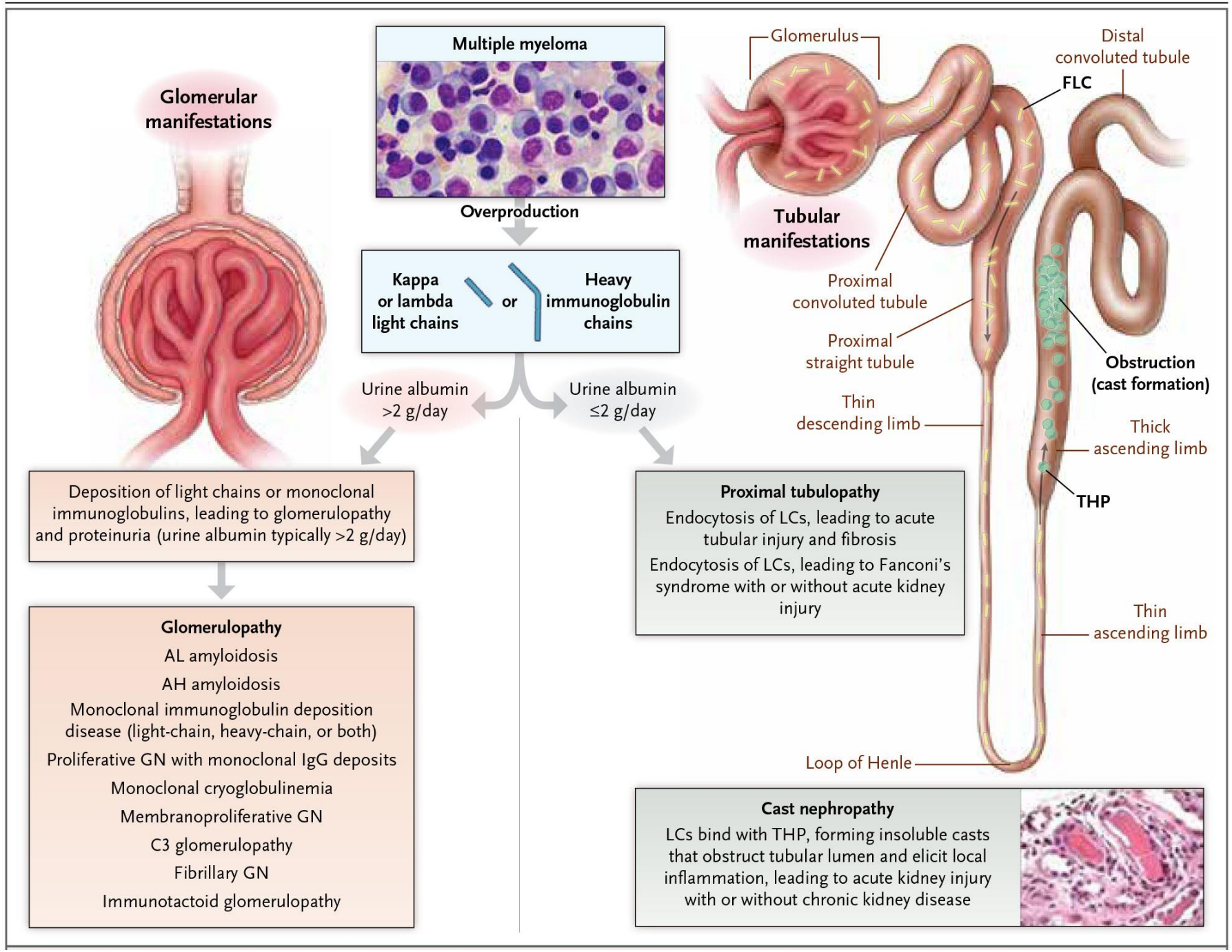
	Type I Cancer Drug–Induced TMA	Type II Cancer Drug–Induced TMA
	Chemotherapy regimen	Anti-VEGF therapy
Characteristic agent	Mitomycin C and/or gemcitabine	Bevacizumab
Onset	Delayed; usually 6-12 mo after starting therapy	Occurs any time after the initiation of treatment and may be involved after prolonged treatment (1 dose to 29 mo)
Dose effect	Cumulative, dose related	Not dose related
Clinical	Appears to be permanent and irreversible; hematologic manifestations usually present; hypertension, acute renal failure, pulmonary edema, and ARDS are common	High likelihood of recovery after interruption (reversible); hematologic manifestations only in half of pts; hypertension, and varying degrees of proteinuria usually without kidney failure
Effect of rechallenge	High probability of recurrent dysfunction that is progressive; may result in intractable kidney failure	Some evidence for the relative safety of rechallenge (additional data needed)
Pathologic	Arteriolar and glomerular capillary thrombosis	Exclusive glomerular capillary thrombosis
Therapy and prognosis	High incidence of acute mortality (4-month mortality up to 75%) and chronic kidney disease requiring dialysis despite drug discontinuation, steroids, or plasma exchange before rituximab and eculizumab use	Patient and kidney survival rates are excellent after stopping drug in association with antihypertensive drugs

Table 3. Emerging Therapies for Cancer Drug–Induced TMA [121-123;126,133]

	Case n	Malignancy	Regimen Inducing TMA	ADAMST13 Level	Prior TMA Therapy	Doses Given	Outcome
Rituximab (375 mg/m^2/wk)	4	Breast, pancreas, lung	MMC- or Gem-based; other: Platins, BVZ	≥38%	Steroids + daily plasma exchange (n, 8->120)	2-8	TMA resolution in 3 cases (2 pts at 5 mo and 1 pt continued to require 3×/wk hemodialysis at 4 mo)
Eculizumab (900 mg)	1	Duodenal	Gem	88%	Steroids + daily plasma exchange (n = 12), then rituximab (375 mg/m^2/wk, 2 doses)	4	Rapid normalization of platelet count, improvement of kidney function, and independence from hemodialysis
Recombinant human soluble thrombomodulin (rTM, 380 U/kg/d)	1	Lung	Gem + BVZ	61%	Concomitant fresh frozen plasma (4 units/d)	6	Patient recovered from TTP and was discharged 1 mo after the onset of TTP-1 year

Abbreviations: BVZ, bevacizumab; Gem, gemcitabine; MMC, mitomycin C; pt, patient; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura.


Amyloidosis
Multiple Myeloma
Imunotactoid GN
Fibrillary GN
Gamma Globulin
Dyscrasias
Monoclonal vs Polyclonal
Light vs Heavy Chain
Gammopathy
SPE / Immunofixatio n
LCDD, HCDD
NephroTube
www.NephroTubeCNE.com

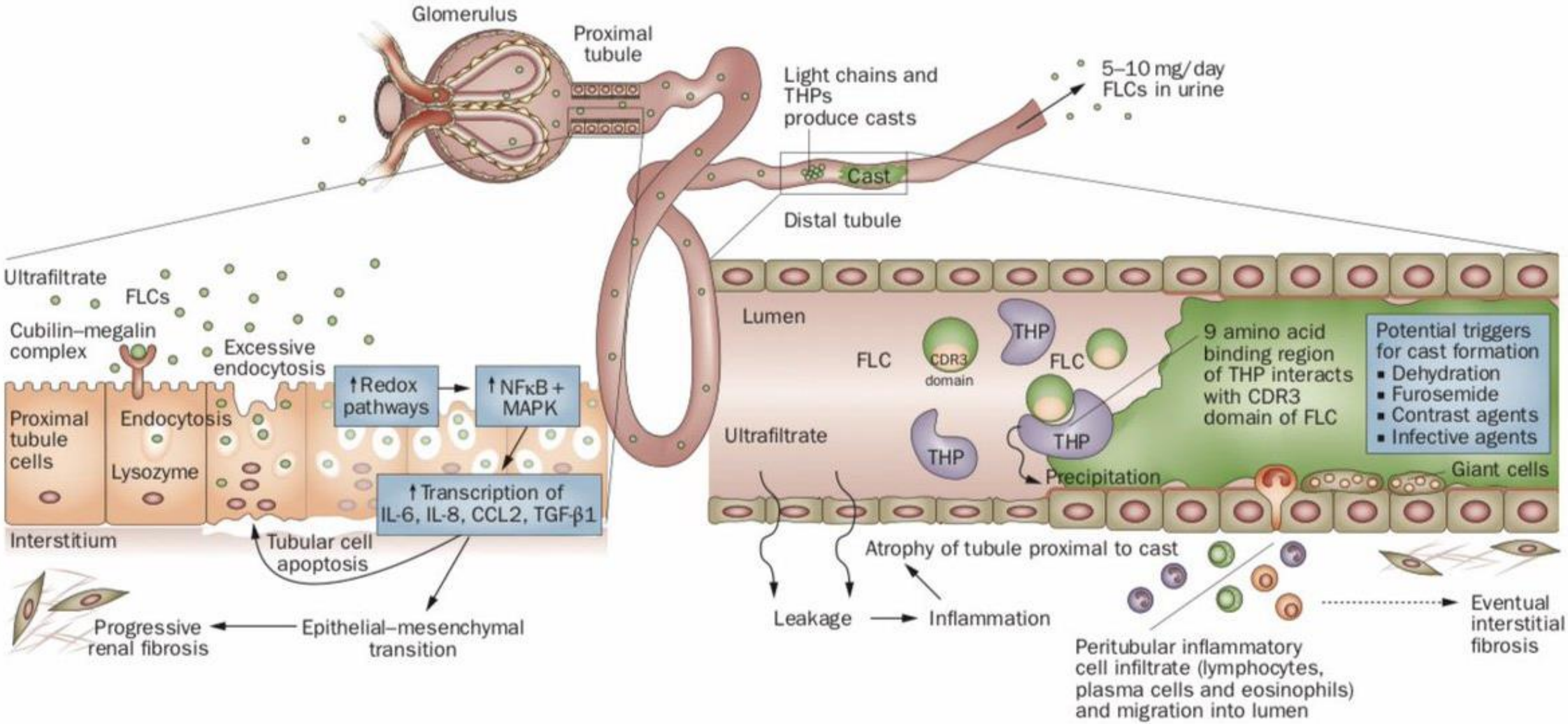

Glomerular manifestations
Multiple myeloma
Overproduction
Kappa or lambda light chains
or
Heavy immunoglobulin chains
Urine albumin >2 g/day
Urine albumin ≤2 g/day
Deposition of light chains or monoclonal immunoglobulins, leading to glomerulopathy and proteinuria (urine albumin typically >2 g/day)
Glomerulopathy
AL amyloidosis
AH amyloidosis
Monoclonal immunoglobulin deposition disease (light-chain, heavy-chain, or both)
Proliferative GN with monoclonal IgG deposits
Monoclonal cryoglobulinemia
Membranoproliferative GN
C3 glomerulopathy
Fibrillary GN
Immunotactoid glomerulopathy
Glomerulus
Distal convoluted tubule
FLC
Tubular manifestations
Proximal convoluted tubule
Proximal straight tubule
Thin descending limb
Obstruction (cast formation)
Thick ascending limb
THP
Thin ascending limb
Loop of Henle
Proximal tubulopathy
Endocytosis of LCs, leading to acute tubular injury and fibrosis
Endocytosis of LCs, leading to Fanconi's syndrome with or without acute kidney injury
Cast nephropathy
LCs bind with THP, forming insoluble casts that obstruct tubular lumen and elicit local inflammation, leading to acute kidney injury with or without chronic kidney disease

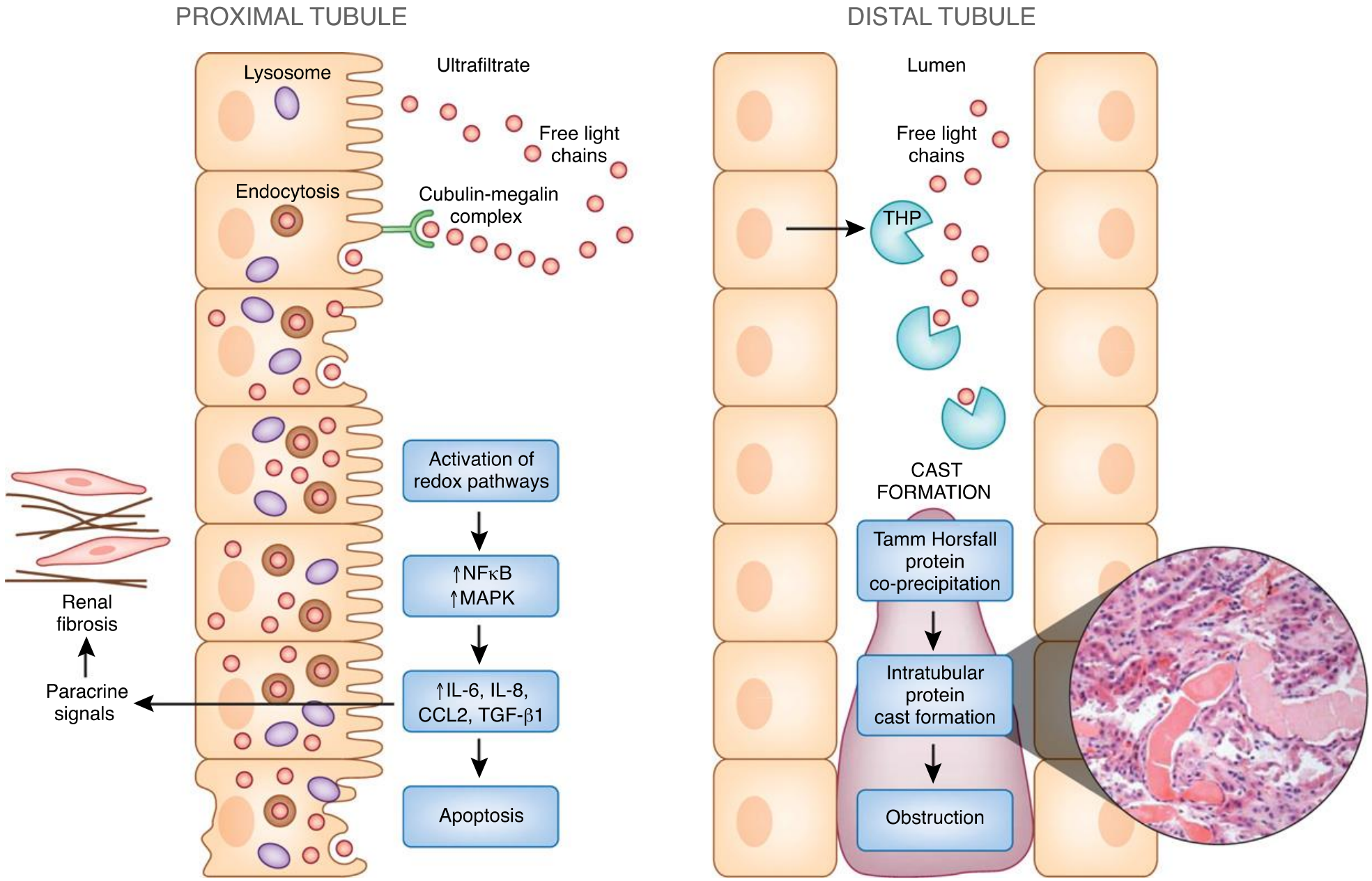
- Patients with multiple myeloma represent an important subclass of patients with hematological malignancies that are prone to develop AKI.

- AKI is quite common, complicating the course of myeloma
  - in up to 20% to 50% of cases

Etiologies of AKI in MM

Paraprotein-related	Metabolic disturbances
Light chain cast nephropathy	Hypercalcemia secondary to bone involvement
Light chain related proximal tubular injury with or without Fanconi syndrome	Hyperuricemia with large tumor burden
Light chain deposition disease	
Amyloidosis (more common with lambda light chains)	


Glomerulus
Proximal tubule
Light chains and THPs produce casts
5–10 mg/day FLCs in urine
Cast
Distal tubule
Ultrafiltrate
FLCs
Cubilin–megalin complex
Excessive endocytosis
Proximal tubule cells
Endocytosis
Lysozyme
↑Redox pathways
↑NFκB + MAPK
↑Transcription of IL-6, IL-8, CCL2, TGF-β1
Interstitium
Tubular cell apoptosis
Progressive renal fibrosis
Epithelial–mesenchymal transition
Lumen
FLC
CDR3 domain
THP
FLC
9 amino acid binding region of THP interacts with CDR3 domain of FLC
Potential triggers for cast formation
▪ Dehydration
▪ Furosemide
▪ Contrast agents
▪ Infective agents
Ultrafiltrate
THP
THP
Precipitation
Giant cells
Atrophy of tubule proximal to cast
Leakage
Inflammation
Eventual interstitial fibrosis
Peritubular inflammatory cell infiltrate (lymphocytes, plasma cells and eosinophils) and migration into lumen


PROXIMAL TUBULE
DISTAL TUBULE
Lysosome
Ultrafiltrate
Free light chains
Endocytosis
Cubulin-megalin complex
Activation of redox pathways
↑NFκB
↑MAPK
↑IL-6, IL-8, CCL2, TGF-β1
Apoptosis
Renal fibrosis
Paracrine signals
Lumen
Free light chains
THP
CAST FORMATION
Tamm Horsfall protein co-precipitation
Intratubular protein cast formation
Obstruction

Indications for Plasma-pheresis

Disease (ASFA* Category)	
TTP/HUS (I)	Thrombotic Thrombocytopenic Purpura – Hemolytic Uremic Syndrome. Thrombocytopenia, hemolytic anemia, neurologic symptoms. Substitution of FFP is therapeutic desired.
Goodpasture Syndrome (I)	Rapid progressive glomerulonephritis and lungs bleeding. Prognostic important early indication to plasmapheresis in combination with Immunsuppressive therapy.
Guillain-Barré-Syndrome (I)	Acute inflammatory attack of myelin sheat in peripheral nerves and spinal ganglions through IgG-Antibodies and immuno-complexes. Ascending paralysis of extremities and trunk up to respiratory paralysis.
Myasthenia Gravis (I)	IgG-Autoantibodies against Acetylcholin rezeptors of skeletal muscles. Neuro-muscular symptoms. Myasthenic crises with respiratory paralysis.
Hyperviscosity Syndrome (I)	High blood viscosity e.g. in M. Waldenström, Myeloma, Cryoglobulinemia. Neurologic and hematologic disturbances, organ damage.
Cryoglobulinemia (I)	Immunglobulin complexis which precipitate in coldness. Skin bleeding closed to fingers and toes, articulation pain, glomerulonephritis.
Renal Transplantation (I)	In acute antibody-mediated rejection to remove anti-HLA antibodies. Also in desensitization for AB0-incompatible and hypersensitized patients before transplantation.
SLE (II)	Systemic Lupus Erythematodes. Autoimmuno desease of skin and vessels with deposition of immuno-complexes composed by DNA and DNA-Antibodies.
Multiple Myeloma (II)	Plasmacytoma. Plasma cell carcinoma which produce abnormal antibodies in bone marrow. The pathologic antibodies cause casts in Kidney. Changes in marrow cause bone damage and hypercalcemia.
Multiple Sclerosis (II)	Type of inflammation of CNS (inflammatory demyeliting disease) in which myelin sheath of brain and spine are damaged. Course of the disease can differ very much with wide range of neurologic symptoms.
Poisoning, Overdose (II)	Mushrooms, snakebite, cisplatin, digoxin

*ASFA = American Society for Apheresis

Kidney International, Vol. 33 (1988), pp. 1175–1180

Controlled plasma exchange trial in acute renal failure due to multiple myeloma

PIETRO ZUCCHELLI, SONIA PASQUALI, LEONARDO CAGNOLI, and GIUSEPPE FERRARI

Department of Nephrology, Malpighi Hospital, U.S.L. 28 Bologna North, Bologna, Italy

Controlled plasma exchange trial in acute renal failure due to multiple myeloma. We studied 29 patients affected by acute renal failure due to multiple myeloma with Bence-Jones proteinuria > 1 g/day to evaluate the effectiveness of plasma exchange in the treatment of severe myeloma nephropathy. Renal failure was severe enough to require dialysis in 24 cases, while the remaining 5 patients showed serum creatinine levels greater than 5 mg/dl. The patients were randomly allocated to Group I (15 patients undergoing plasma exchange together with corticosteroids, cytotoxic drug, hemodialysis only when needed) or to Group II (14 patients undergoing peritoneal dialysis together with corticosteroids and cytotoxic drug). In Group I Bence-Jones proteinuria decreased dramatically ($P < 0.01$) with a significant increase in urine output ($P < 0.001$), while Group II presented a slight reduction in Bence-Jones proteinuria without a significant increase in daily diuresis. Thirteen out the 15 Group I patients recovered renal function reaching serum creatinine levels ≤2.5 mg/dl in most cases. Only two patients in Group II improved renal failure well enough to stop dialysis. The one-year survival rate was significantly higher in Group I (66%) than in Group II (28%, $P < 0.01$). We conclude that plasma exchange associated to chemotherapy rapidly removes large amounts of light chains, improves both renal function and long-term survival expectancies.

Annals of Internal Medicine | ARTICLE

Plasma Exchange When Myeloma Presents as Acute Renal Failure

A Randomized, Controlled Trial

William F. Clark, MD; A. Keith Stewart, MD; Gail A. Rock, MD; Marion Sternbach, MD; David M. Sutton, MD; Brendan J. Barrett, MD; A. Paul Heidenheim, MA; Amit X. Garg, MD; David N. Churchill, MD; and the Canadian Apheresis Group

Background: Two small, randomized trials provide conflicting evidence about the benefits of plasma exchange for patients with acute renal failure at the onset of multiple myeloma.

Objective: To assess the effect of 5 to 7 plasma exchanges on a composite outcome in patients with acute renal failure at the onset of multiple myeloma.

Design: Randomized, open, controlled trial, stratified by chemotherapy and dialysis dependence, conducted from 1998 to 2004.

Setting: Hospital plasma exchange units in 14 Canadian medical centers.

Participants: 104 patients between 18 and 81 years of age with acute renal failure at the onset of myeloma.

Intervention: Study participants were randomly assigned to conventional therapy plus 5 to 7 plasma exchanges of 50 mL per kg of body weight of 5% human serum albumin for 10 days or conventional therapy alone. Ninety-seven participants completed the 6-month follow-up.

Measurements: The primary outcome was a composite measure of death, dialysis dependence, or glomerular filtration rate less than 0.29 $mL \cdot s^{-2} \cdot m^{-2}$ (<30 mL/min per 1.73 m^2).

Results: At enrollment, the plasma exchange and control groups were similar for dialysis dependence, chemotherapy, sex, age, hypercalcemia, serum albumin level, 24-hour urine protein level, serum creatinine level, and Durie–Salmon staging. The primary composite end point occurred in 33 of 57 (57.9%) patients in the plasma exchange group and in 27 of 39 (69.2%) patients in the control group (difference between groups, 11.3% [95% CI, −8.3% to 29.1%]; $P = 0.36$). One third of patients in each group died.

Limitations: The study was small, used a composite outcome, and did not use renal biopsy as an inclusion criterion. Recruiting physicians were blinded to treatment allocation but not to treatment thereafter.

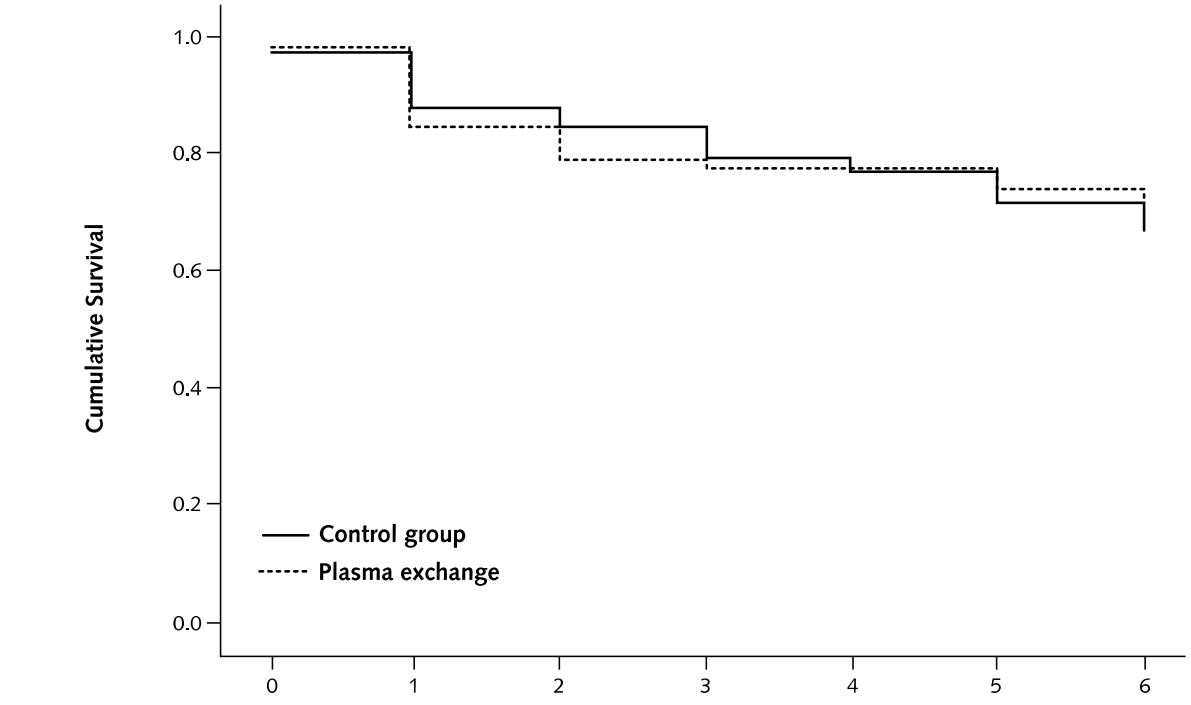
Conclusions: In patients with acute renal failure at the onset of multiple myeloma, there is no conclusive evidence that 5 to 7 plasma exchanges substantially reduce a composite outcome of death, dialysis dependence, or glomerular filtration rate less than 0.29 $mL \cdot s^{-2} \cdot m^{-2}$ (<30 mL/min per 1.73 m^2) at 6 months.

Ann Intern Med. 2005;143:777-784. www.annals.org

For author affiliations, see end of text.

ClinicalTrials.gov identifier: NCT00120263.

No difference on M&M's



Patients at risk, *n*							
Control group	39	37	34	33	31	30	28
Plasma exchange	58	56	49	46	45	44	42

modialysis International 2010; **14**:355–363

Role of plasmapheresis in the management of myeloma kidney: A systematic review

Diptesh GUPTA,[1] Lohith BACHEGOWDA,[2] Gautam PHADKE,[1,3] Sue BOREN,[4,5] Diane JOHNSON,[6] Madhukar MISRA,[1,3]

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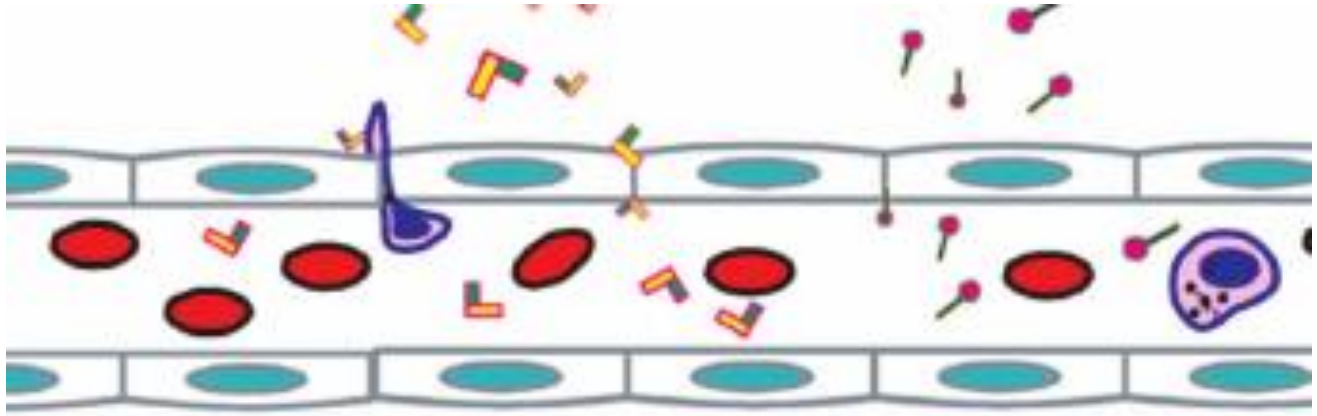
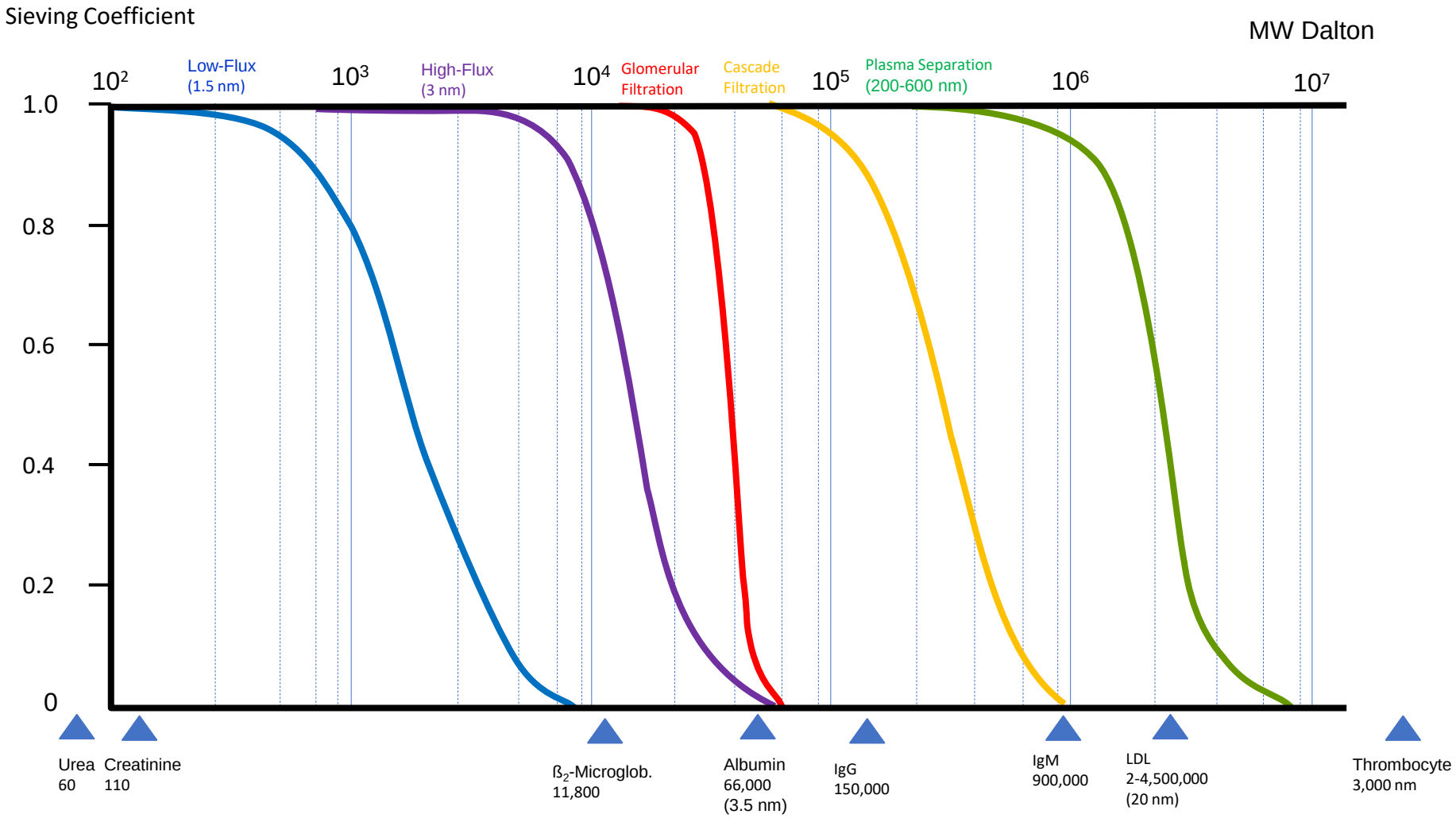
Abstract

Multiple myeloma complicated by acute renal failure is a diagnosis often encountered by the practicing nephrologist. The role of plasmapheresis in such patients has been of interest for decades. Three randomized controlled trials (RCTs) and multiple observational trials have evaluated the potential role of plasmapheresis in the management of this condition. This systematic review presents the results of these trials regarding survival benefits, recovery from dialysis, and improvement in renal function. A comprehensive search revealed 56 articles. Of these, only 8 articles met our inclusion criteria (3 RCTs, 1 correction of results, and 4 observational trials). Two of the 3 RCTs showed no difference in survival benefit. Two of the 3 RCTs showed a greater percentage of patients stopping dialysis in the intervention group; however, these results were not reproduced in the largest trial. All the studies showed an improvement in renal function for patients receiving plasmapheresis; however, only 2 RCTs and 1 retrospective study showed a statistically significant improvement in renal function among patients who received plasmapheresis in comparison with a control group. Our systematic review does not suggest a benefit of plasmapheresis independent of chemotherapy for multiple myeloma patients with acute renal failure in terms of overall survival, recovery from dialysis, or improvement in renal function.

Rebound of FLC



Sieving Coefficient



http://www.revistanefrologia.com

originals

See editorial comment on page 15

Haemodialysis using high cut-off dialysers for treating acute renal failure in multiple myeloma

Guillermo Martín-Reyes[1], Remedios Toledo-Rojas[1], Álvaro Torres-Rueda[1], Eugenia Sola-Moyano[1], Lourdes Blanca-Martos[1], Laura Fuentes-Sánchez[1], M. Dolores Martínez-Esteban[1], M. José Díez-de los Ríos[2], Alicia Bailén-García[3], Miguel González-Molina[1], Isabel García-González[4]

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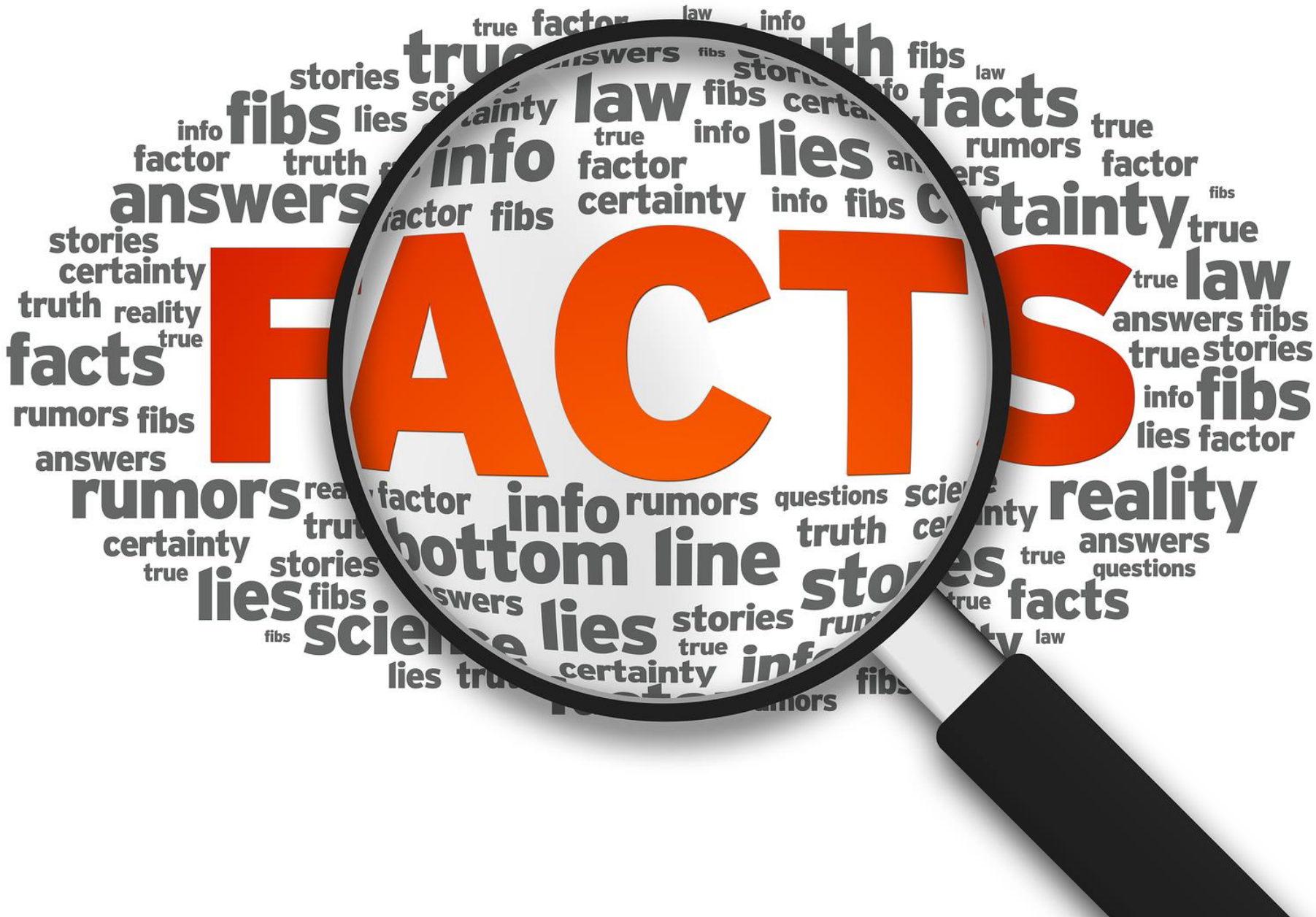
[2] Laboratorio de Análisis Clínicos. Hospital Regional Universitario Carlos Haya. Málaga. Spain
[3] Servicio de Hematología. Hospital Regional Universitario Carlos Haya. Málaga. Spain
[4] Servicio de Anatomía Patológica. Hospital Regional Universitario Carlos Haya. Málaga. Spain

- Effective chemo-therapy regimens include **proteasome inhibitors such as bortezomib** along **with other agents** such as **thalidomide, corticosteroids, vincristine, and adriamycin in various combinations**

- Bortezomib has the added benefit of acting quickly to improve glomerular filtration rate (GFR) with a median time of response at 1.34 months

Should Dialysis be offered to cancer pts with severe AKI ?


FACTS
true
factor
law
info
fibs
facts
stories
lies
truth
answers
certainty
rumors
reality
bottom line
questions
science

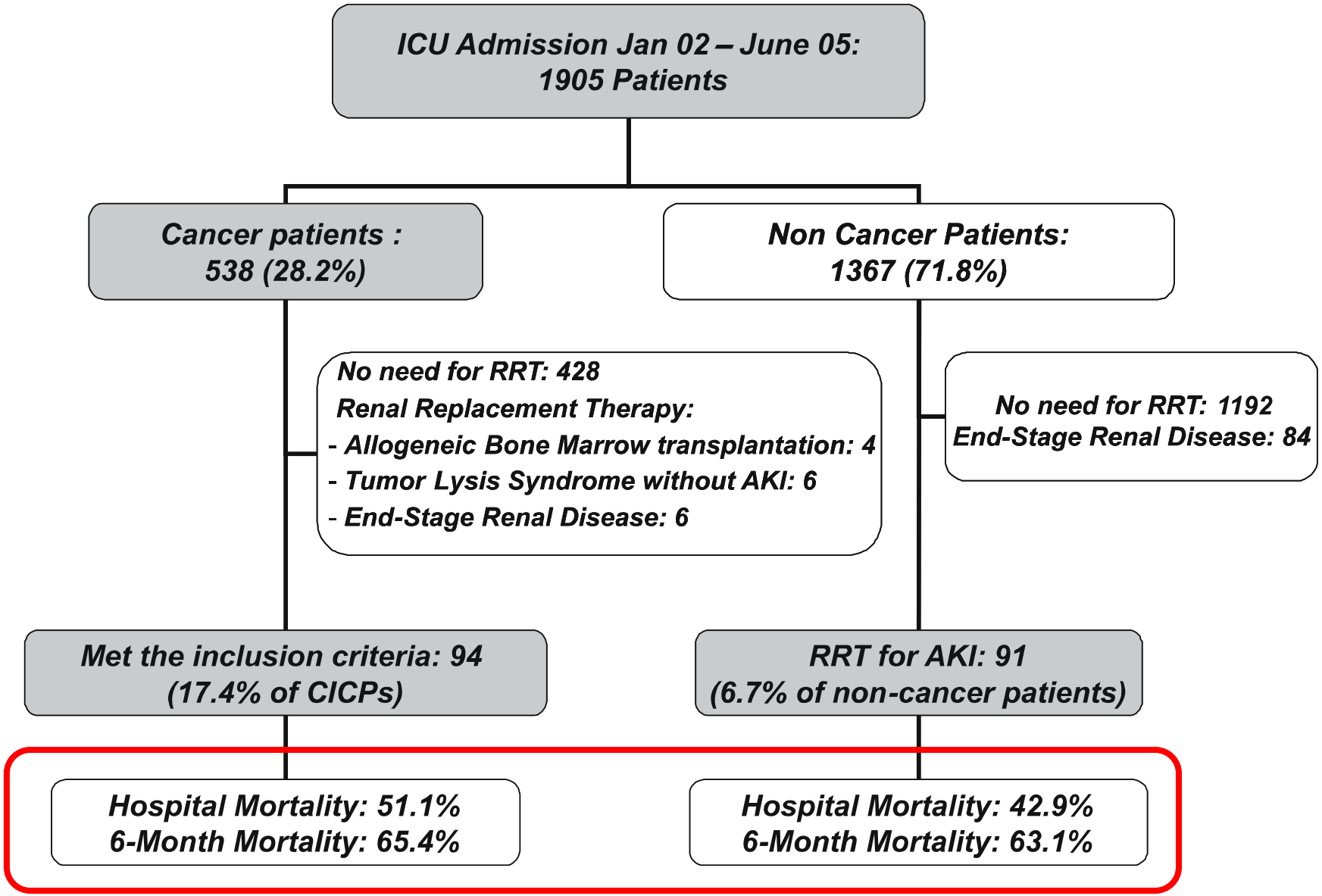
- AKI + Cancer = mortality & morbidity +++
- AKI + Cancer requiring RRT >>> not uncommon in ICU
- AKI + Cancer + RRT = very high mortality (up to 85% in HCT)

Intensive Care Med (2007) 33:765–772
DOI 10.1007/s00134-007-0579-1

ORIGINAL

Michael Darmon
Guillaume Thiery
Magali Ciroldi
Raphaël Porcher
Benoît Schlemmer
Élie Azoulay

Should dialysis be offered to cancer patients with acute kidney injury?


ICU Admission Jan 02 – June 05:
1905 Patients
Cancer patients :
538 (28.2%)
Non Cancer Patients:
1367 (71.8%)
No need for RRT: 428
Renal Replacement Therapy:
- Allogeneic Bone Marrow transplantation: 4
- Tumor Lysis Syndrome without AKI: 6
- End-Stage Renal Disease: 6
No need for RRT: 1192
End-Stage Renal Disease: 84
Met the inclusion criteria: 94
(17.4% of CICPs)
RRT for AKI: 91
(6.7% of non-cancer patients)
Hospital Mortality: 51.1%
6-Month Mortality: 65.4%
Hospital Mortality: 42.9%
6-Month Mortality: 63.1%

In selected cancer populations,
full ICU management (RRT)
leads to meaningful survival

Take Home Messages

- AKI + Cancer = frequent complications
- AKI + Cancer = increased M&M's
- AKI + Cancer = increased LOS
- AKI + Cancer = interruptions in cancer ttt / complicates the management of cancer pts.
- AKI in Cancer >>> usual causes & specific causes (mostly multifactorial)
- Prognosis >>> related to number of organs dysfunctions
- Do not deprive RRT to a cancer pt just because he/she has cancer !

MERCI