Chapitre 7 : L'épuration extra-rénale.

Troisième question de la conférence de consensus

Quel support utiliser pour l'épuration extra-rénale, dans quels conditions et environnement ?

Trente-six études étaient éligibles pour la revue systématique. Elles n'ont pas évalué de manière adéquate les modalités de remplacement extra-rénal (EER), le moment de son initiation et l'impact de ces stratégies sur les résultats des patients.

Hémopathies malignes

References	Type of study	Uni/Multi	BMT	Type of dialysis	Reason for dialysis	ARF Aetiology	Dialysis location
BENOIT et al, 2005 [316]	R	Uni	Allo	Mixed	Not specified	Not specified	ICU
BRIDOUX et al, 2017 [317]	P randomised	Multi	No	Mixed	Mixed	Other	Not specified
CANET et al, 2013 [318]	P non-randomised	Uni	Not specified	Mixed	Not specified	Not specified	ICU
COSIO et al, 1981 [319]	R	Uni	No	Intermittent HF	Not specified	Other	Nephrology
DARMON et al, 2015 [241]	P (retrolective analysis)	Multi	Allo + auto	Mixed	Not specified	Mixed	ICU
FLORES et al, 2008 [320]	Cohort	Multi	Type of graft not specified	CVVHDF	Mixed	Mixed	ICU
GILBERT et al, 2013 [307]	R	Uni	Allo + auto	CVVHDF	Not specified	Not specified	ICU
GRUSS et al, 1998 [321]	R	Uni	Allo	Not specified	Not specified	Not specified	Not specified
LANORE et al, 1991 [322]	R	Uni	Not specified	Not specified	Mixed	Mixed	ICU
LETOURNEAU et al, 2002 [323]	R	Uni	Allo + auto	Mixed	Mixed	Mixed	ICU
PARK et al, 2011 [324]	R	Uni	Type of graft not specified	CVVHDF	Mixed	Other	ICU
SMOYER et al, 1995 [325]	R	Uni	Allo	Mixed	Mixed	Other	ICU

Résultats

References	N patients	Dialysis independence rate	Chronic dialysis rate	Hospital death rate* (%)	Remarks
BENOIT et al, 2005 [316]	50	-	-	41/49 (83.7%)	-
BRIDOUX et al, 2017 [317]	98	41.3% vs 27.1% At 3 months	-	-	Prognostic factors for dialysis independence in univariate analysis: type and rate Immunoglobulin and type of membrane for dialysis
CANET et al, 2013 [318]	72	61.1%	38.9%	85.7%	-
COSIO et al, 1981 [319]	24	8.3% (?)	29.2%	-	-
DARMON et al, 2015 [241]	271	-	12.9%	155/271 (57.2%)	-
FLORES et al, 2008 [320]	51	-	-	23/51 (45.1%)	Paediatric ICU mortality
GILBERT et al, 2013 [307]	20	-	-	18/20 (90%)	-
GRUSS et al, 1998 [321]	21	-	-	17/21 (81%)	-
LANORE et al, 1991 [322]	43	-	-	18/43 (41.9%)	ICU mortality
LETOURNEAU et al, 2002 [323]	14	-	-	-	-
PARK et al, 2011 [324]	94	77.3%	5.3% (?)	76.6%	ICU mortality
SMOYER et al, 1995 [325]	98 (14 haematological)	-	-	9/13 (69.2%)	-

*Number of death/number of assessed patients

Séries mixtes

References	Type of study	Uni/Multi	BMT/Metastatic	Type of dialysis	Reason for dialysis	ARF Aetiology	Dialysis location
BAUMGARTNER et al, 1976 [336]	R	Uni	No graft/ not specified	Intermittent HF	Not specified	Mixed	Not specified
BECKLEY et al, 1982# [337]	R	Uni	Not specified	Intermittent HF	Mixed	Not specified	Not specified
BERGHMANS et al, 2004 [338]	R	Uni	Allo/Mixed	CVVHDF	Mixed	Mixed	ICU
DARMON et al, 2007 [339]	Cohort	Uni	Not specified / Not specified	Mixed	Mixed	Mixed	ICU
FISCHLER et al, 2016 [64]	R	Uni	Allo + auto/mixed	CVVHDF	Mixed	Mixed	ICU
GARIMELLA et al, 2017* [340]	Database	Multi	Not specified	Not specified	Not specified	Tumour lysis syndrome	Not specified
LANE et al, 1994 [341]	R	Uni	Allo + auto/ Not specified	Mixed	Mixed	Mixed	Not specified
MACCARIELLO et al, 2011 [342]	Cohort	Multi	Not specified / Mixed	Mixed	Mixed	Other	ICU
SALAHUDEEN et al, 2009 [343]	R	Uni	Allo/ Not specified	SLEDD	Anuria	Other	ICU
SOARES et al, 2010* [344]	P non-randomised	Multi	Not specified	Not specified	Not specified	Not specified	ICU
SOARES et al, 2006 [286]	P non-randomised	Uni	Not specified/ Not specified	Mixed	Not specified	Other	ICU

Résultats

References	N patients	Dialysis independence rate	Hospital Mortality	Prognostic factors for hospital mortality (Multivariate)
BAUMGARTNER et al, 1976 [336]	31	-	-	-
BECKLEY et al, 1982 [337]	70	65.7%	-	-
BERGHMANS et al, 2004 [338]	32	59.4%	53.1%	N failing organs
DARMON et al, 2007 [339]	94	-	51.1%	-
FISCHLER et al, 2016 [64]	103	43.7%	63.1%	N failing organs, Hypoalbuminemia
GARIMELLA et al, 2017 [340]	2919	-	-	Need for dialysis = pejorative factor
LANE et al, 1994 [341]	30	23.3%	90%	-
MACCARIELLO et al, 2011 [342]	118	84.6%	78%	N failing organs
SALAHUDEEN et al, 2009 [343]	199	22.6%	65.3%	-
SOARES et al, 2010 [344]	87 of whom 31 dialyses	-	38.5%	-
SOARES et al, 2006 [286]	98	-	70.4%	-

Dans notre expérience

Tableau 3

Résultats des études réalisées sur les techniques de support vital.

Technique	Années de recrutement et référence	N patients	Survie hospitalière	Facteurs prédictifs survie hospitalière
Réanimation cardiorespiratoire	1985-1992[7]	49	10 %	
Ventilation mécanique invasive (VMI)	1985-1997[8]	168	17 %	IGS II Leucopénie
Ventilation non invasive (VNI)	2000-2001[9]	40	42,5 %	
VMI à l'ère VNI	2000-2007[11]	164	24 %	VMI après échec VNI Leucopénie Bilirubinémie
Epuration extra-rénale (1)	1997-2002[15]	32	47 %	Nombre organes défaillants
Epuration extra-rénale (2)	2003-2012[16]	103	37 %	Nombre organes défaillants Hypoalbuminémie

IGS II : indice de gravité simplifié II ; VMI : ventilation mécanique invasive ; VNI : ventilation non invasive

l'EER est efficace

Support Care Cancer (2004) 12:306–311
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ORIGINAL ARTICLE

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Continuous venovenous haemofiltration in cancer patients with renal failure: a single-centre experience

Table 1 Characteristics of the 32 eligible cancer patients treated by continuous venovenous hemodiafiltration (CVVHDF) for acute renal failure

Patients characteristics	Number
Gender (male/female)	23/9
Median age (range)	61 (33–84)
Causes of admission to ICU	
Renal failure	17
Respiratory	11
Cardiovascular complications	1
Infectious disease	3
General gravity scores: median (range)	
APACHE II	31 (19–44)
IGS II	67 (31–103)
Number of organ failures (including kidney)	
1	10
2	6
3	13
4	2
pH (median/range)	7.34 (7.11–7.47)
Creatinine (median/range) (μmol/l)	424.3 (194.5–1290.6)
Potassium (median/range) (mEq/l)	4.1 (3.3–7.4)

Table 2 Cancer characteristics in 32 patients with acute renal failure

Patients characteristics	Number
Haematological malignancies	16
Acute myeloid leukemia	3
Acute lymphoblastic leukemia	2
Chronic leukemia	5
Lymphoma	3
Myelodysplasia	2
Multiple myeloma	1
Solid tumours (limited/metastatic)	12/4
Lung	4
Digestive tract	5
Bladder	3
Other	4
Cancer status	
Remission complete/partial	8/2
No change	2
Progressive disease	6
Induction treatment	14
Neoplastic disease phase	
Diagnostic	3
Curative	17
Controllable	12

Table 3 Results of univariate prognostic factors analysis included in the multivariate models for hospital mortality

	Dead during hospital stay		*P* value
	Yes	No	
Haematological malignancies (*n*)	11	5	0.08
Solid tumours (*n*)	6	10	-
Immunosuppressed (*n*)	14	8	0.08
Others (*n*)	3	7	-
Renal failure aetiology (*n*)	-	-	0.01
Renal (*n*)	17	10	-
Other (*n*)	0	5	-
Bone marrow transplantation (*n*)	8	1	0.01
Others (*n*)	9	14	-
Number of organ failures	-	-	0.0001
1	0	10	-
>1	16	5	-
Age (median-years)	56	65	0.03
APACHE II	34	25	0.006
IGS II	76	47	0.01
ARDS (*n*)	7	0	0.005
No ARDS (*n*)	10	15	-
Mechanical ventilation (*n*)	12	3	0.004
No mechanical ventilation (*n*)	5	12	-
Systolic blood pressure (median mm Hg)	115	149	0.09
Neutrophil count (median mm^3)	3,205	4,750	0.18
Lymphocyte count (median mm^3)	275	550	0.02
Bilirubin (median μmol/l)	61.6	18.8	0.001
Creatinine (median μmol/l)	318.2	565.8	0.009
Bicarbonate (median mEq/l)	18	20	0.15
Phosphate (median mmol/l)	1.8	2.2	0.16
Thromboplastin time (median INR)	1.4	1.1	0.03

account either APACHE II or IGS II. Only the number of organ failures was found as a statistically significant prognostic factors in the two models (β=–0.79, p=0.009 and β=–0.77, p=0.01), meaning that when only renal failure occurred, the prognosis was better than if other organ failures were associated. None of the ten patients with only renal failure died at the difference of 16 among the 21 patients with more than one organ failure. High phosphate level was also found a significant prognostic factor in the model including APACHE II (β=0.38; p=0.04).

frontiers in Medicine

ORIGINAL RESEARCH
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CrossMark

Continuous Renal Replacement Therapy for Acute Renal Failure in Patients with Cancer: A Well-Tolerated Adjunct Treatment

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TABLE 1 | Characteristics at ICU admission of 103 patients with cancer with acute renal failure requiring renal replacement therapy.

Sex (male/female)	69/34 (67%/33%)
Age (median/range)	62 years (19–87)
Solid malignancies (locoregional/metastatic)	68 (66%) (28/40)
Breast	7 (7%)
Lung	6 (6%)
Digestive tract	15 (15%)
Prostate/bladder/kidney	23 (22%)
Other	17 (17%)
Hematological malignancies	35 (34%)
Leukemia	10 (10%)
Lymphoma	14 (14%)
Multiple myeloma	9 (9%)
Myelodysplastic syndrome	2 (2%)
Stem cell transplantation before ICU admission (allo/auto)	18 (14/4) (17%)
Cancer phase	
Diagnostic	9 (9%)
Curative	41 (40%)
Controllable	53 (51%)

TABLE 2 | Principal etiologies of acute renal failure in patients admitted in the ICU.

	n	%[a]
Nephrotoxic drugs	48	47
Shock/sepsis	41	40
Acute tubular necrosis[b]	19	18
Cancer	10	10
Tumor lysis syndrome	8	8
MOF	4	4
Hepato-renal syndrome	4	4
Other	12	12
Unknown[c]	6	6

[a]One patient could have had more than one etiological factor: a combination of at least two factors has been seen in 43 patients (42% of the cases).

[b]Acute tubular necrosis except nephrotoxic drugs and shock/sepsis.

[c]No aetiology has been formally identified.

MOF, multiple organ failure.

Results: One hundred and three patients are assessed: men/women 69/34, median age 62 years, solid/hematologic tumors 68/35, median SAPS II 56. Mortality rate was 63%. Seven patients required chronic renal dialysis. After multivariate analysis, two variables were statistically associated with hospital mortality: more than one organ failure (including kidney) (OR 5.918; 95% CI 2.184–16.038; $p < 0.001$) and low albumin level (OR 3.341; 95% CI 1.229–9.077; $p = 0.02$). Only minor complications related to CVVHDF have been documented.

TABLE 4 | Summary of publications assessing renal replacement therapy in patients with cancer admitted into ICU.

Reference	Population	*N*	RRT	Mortality	Prognostic factors for hospital mortality
Mixed population (solid and hematological tumors, including bone marrow transplantation)					
Berghmans et al. (15)	Solid: 50% Hemato: 50% BMT: 28%	32	CVVHDF	ICU: 50% Hospital: 53%	Number of organ failure
Salahudeen et al. (5)	Solid: 38% Hemato: 62% BMT: 18%	199	C-SLED	Day 30: 65%	SOFA score, pH, mean blood pressure
Mixed population (solid and hematological tumors, excluding bone marrow transplantation)					
Maccariello et al. (13)	Solid: 73% Hemato: 27%	118	IRRT daily conventional IRRT daily extended CRRT	ICU: 70% Hospital: 78%	Number of organ failure
Darmon et al. (7)	Solid: 7% Hemato: 78% Other: 15%	94	CRRT IRRT	ICU: 43.6% Hospital: 51.1% 6 months: 65.4%	LOD score, late RRT (>24 h after ICU admission)
Soares et al. (14)	Solid: 75% Hemato: 25%	98	IRRT conventional IRRT extended CRRT	Hospital: 64–86%	–
Hematological tumors					
Letourneau et al. (12)	BMT: 100%	14	CVVHDF IRRT	–	–
Lanore et al. (11)	BMT: 11%	43		ICU: 72%	ARF secondary to sepsis, SAPS score, mechanical ventilation support
Benoit et al. (9)	BMT: 22.4%	50	IRRT CRRT	ICU: 79.6% Hospital: 83.7% 6 months: 86%	–

Le pronostic ne dépend pas intrinséquement de l'affection néoplasique sous-jacente

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Advance Access publication 25 January 2005

Nephrology
Dialysis
Transplantation

Original Article

Outcome in critically ill medical patients treated with renal replacement therapy for acute renal failure: comparison between patients with and those without haematological malignancies

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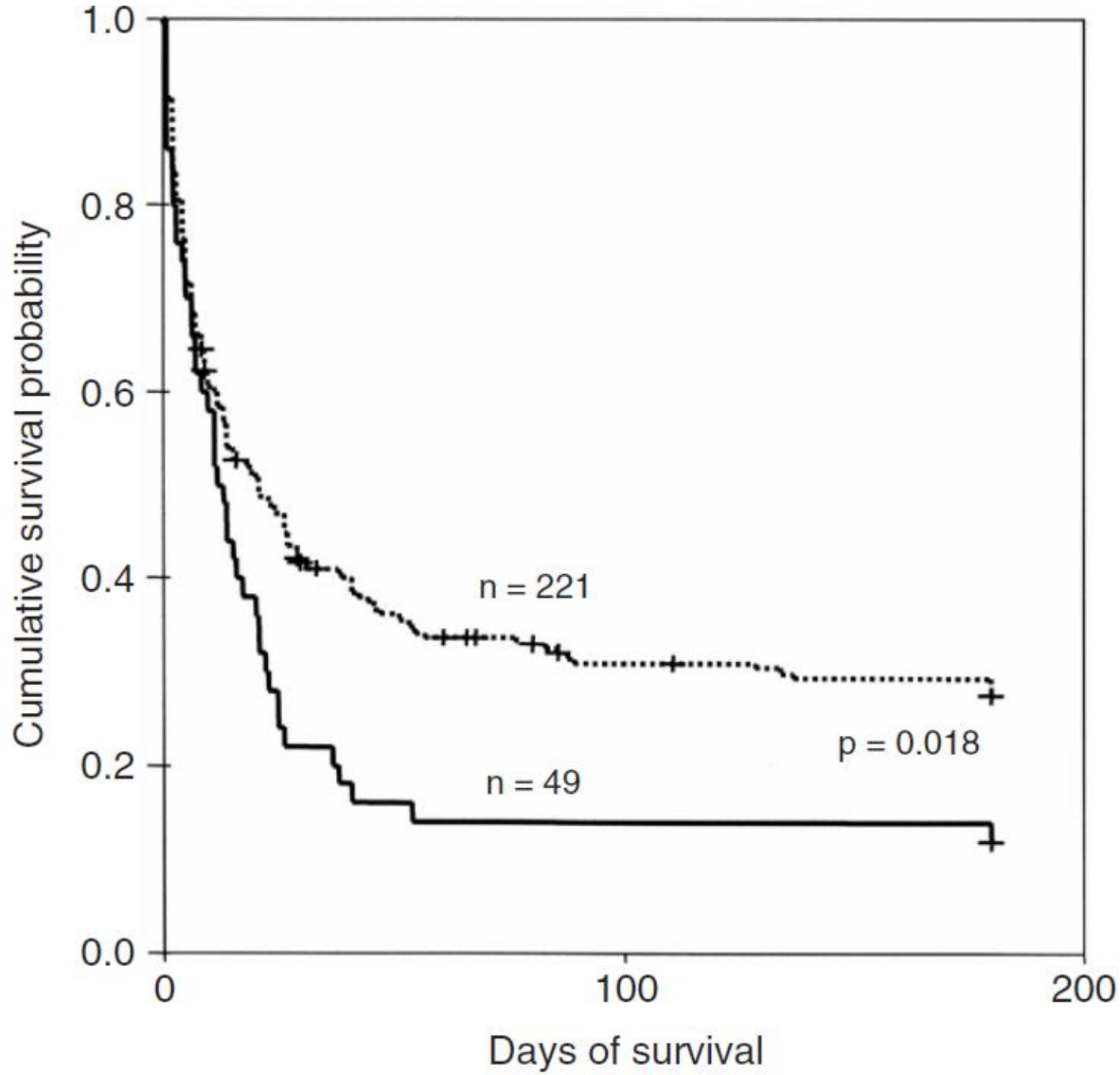

Fig. 1. Kaplan–Meier survival estimates in patients with ($n=49$, solid line) and those without haematological malignancies who received RRT in the ICU ($n=221$, interrupted line).

Table 1. Baseline characteristics and severity of illness in medical ICU patients with and without haematological malignancies who received renal replacement therapy for acute renal failure ($n = 270$)[a]

Variables	Patients with haematological malignancies ($n = 49$)	Patients without haematological malignancies ($n = 221$)	*P*-value
Baseline characteristics			
Gender (male)	31 (63.3%)	135 (61.1%)	0.87
Age (years)	62 (44.1–67.5)	63.3 (52.2–71.7)	0.02
Days of hospitalization before admission	7 (1–21)	0 (0–2)	<0.001
Severity of illness at and during admission			
APACHE II score	30 (23–36)	27 (20–32)	0.019
APACHE II predicted mortality	67.9 (35.3–84.8)	49.5 (24.8–70.3)	0.001
Mechanical ventilation	43 (87.8%)	158 (71.5%)	0.018
Duration of ventilation (days)[b]	10 (2–22)	5 (2–14)	0.063
Vasopressor use	42 (85.7%)	170 (76.9%)	0.248
Use of continuous RRT as initial mode	35 (71.4%)	96 (43.4%)	<0.001
Time from ICU admission to RRT (days)	1 (0–5)	1 (0–4.5)	0.48
Length of stay at the ICU (days)	11 (3–23)	8 (3–20)	0.465

[a]Categorical variables are reported as counts (%) and continuous variables as median (interquartile range).
[b]Among ventilated patients.
The Acute Physiology and Chronic Health Evaluation (APACHE) II score is a severity of illness score. Higher scores indicate a more severe impairment. RRT = renal replacement therapy.

Table 2. Impact of the presence of a haematological malignancy on the outcome in medical ICU patients with acute renal failure who received renal replacement therapy ($n = 270$)[a]

Variables	Univariate		Multivariate	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Baseline characteristics				
Haematological malignancy	1.52 (1.07–2.13)	0.018	–	0.78
Age >65 years	1.20 (0.09–1.59)	0.21	–	0.093
Hospital stay before admission (per day increase)	1.01 (1.01–1.02)	<0.001	1.02 (1.01–1.03)	<0.001
Severity of illness during admission				
APACHE II score (per point increase)	1.05 (1.03–1.06)	<0.001	1.04 (1.02–1.05)	<0.001
Mechanical ventilation	1.92 (1.35–2.73)	<0.001	–	0.35
Vasopressor use	2.51 (1.65–3.82)	<0.001	2.1 (1.38–3.28)	0.001
Use of continuous RRT as initial mode	2.34 (1.75–3.14)	<0.001		

[a]Results are calculated by Cox proportional hazard models. The hazard ratio (95% confidence interval, *P*-value) for haematological malignancy was 1.28 (0.91–1.85, $P = 0.16$) after adjustment for the APACHE II score and 1.33 (0.93–1.89, $P = 0.12$) after adjustment for the duration of hospitalization before ICU admission.

Confirmé dans une population plus générale

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ORIGINAL

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

Table 2 Factors associated with acute kidney injury. *NSAID* non-steroidal anti-inflammatory drug, *ACE* angiotensin-converting enzyme, *DIC* disseminated intravascular coagulation

	Number*
Nephrotoxic agents	39 (41.9)
Vancomycin	24 (25.5)
Aminoglycoside	22 (23.4)
Deoxycholate amphotericin	8 (8.5)
Radiographic contrast agent	4 (4.3)
NSAID	3 (3.2)
ACE inhibitors	2 (2.1)
Methotrexate	2 (2.1)
Cisplatin	1 (1.1)
Sepsis	71 (75.5)
Including septic shock	44 (46.8)
DIC	42 (44.7)
Including malignancy-related DIC	26 (26.7)
Malignancy-related factors	
Acute tumor lysis syndrome	39 (41.5)
Cast nephropathy	10 (10.6)
Infiltration	5 (5.3)
Obstruction	5 (5.3)
Thrombotic microangiopathy	3 (3.2)
Renal amyloidosis	1 (1.1)
Urinary excretion of lysozyme	1 (1.1)
Intravascular hemolysis	1 (1.1)

* Numbers in parentheses are percentages

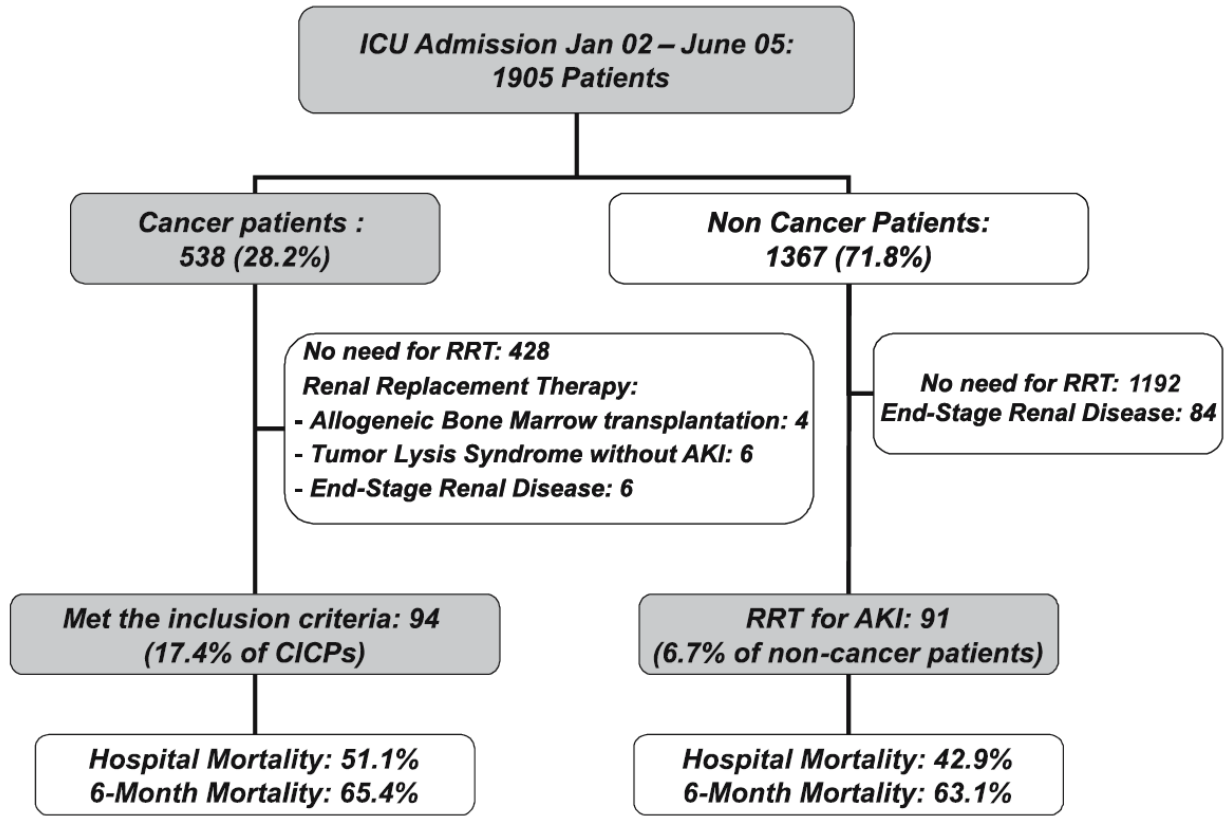

Fig. 1 Flow chart of patients admitted during the study period. The 6-month mortality was calculated on the 78 patients with cancer and 65 patients without cancer who were still available for follow-up. *RRT* renal replacement therapy, *CICPs* critically-ill cancer patients, *AKI* acute kidney injury. End-stage renal disease was defined as previously diagnosed chronic renal failure with an estimated glomerular filtration rate < 15 ml/min)

Table 4 Comparison between critically ill patients with and without cancer. 6-month mortality was calculated on the 78 patients with cancer and 65 patients without cancer who were still available for follow-up. *SAPS II* Simplified Acute Physiology Score

	Cancer ($n=94$)	No cancer ($n=91$)	p-value
Male gender	73 (77.6%)	58 (63.7%)	0.04
Age (years)	53.5 (41-64)	53 (41-66)	0.32
Knaus C or D [24]	29 (30.8%)	20 (22%)	0.17
SAPS II score at ICU admission	53 (40-75)	46 (38-67)	0.27
Length of ICU stay	9 (4-16)	9 (4-17)	0.54
Reasons for ICU admission			0.59
Medical	93 (98.9%)	89 (97.8)	
Surgical	0	1 (1.1%)	
Surgical emergency	1 (1.1%)	1 (1.1%)	
Hospital mortality	48 (51.1%)	39 (42.9%)	0.3
6-month mortality	51 (65.4%)	41 (63.1%)	0.99
Follow-up (days)	51 (12-215)	19 (7-110)	0.03

Table 3 Logistic regression: independent predictors of hospital mortality. [Area under the receiver operating characteristics curve = 0.78 (95% CI, 0.68–0.87); Hosmer–Lemeshow goodness of fit ($\chi^2 = 7.87$; $p = 0.45$)]. *CI* confidence interval, *RRT* renal replacement therapy, *LOD* Logistic Organ Dysfunction score

	Odds ratio	95% CI	*p*-value
Renal function deterioration in the ICU	5.26	1.58-17.52	0.007
Anuria at ICU admission	2.41	0.91-6.42	0.076
LOD (per point)	1.31	1.11-1.55	0.002

Il existe un risque de dialyse chronique

VOLUME 24 · NUMBER 24 · AUGUST 20 2006

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prognosis of Critically Ill Patients With Cancer and Acute Renal Dysfunction

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A B S T R A C T

Purpose

To evaluate the outcomes of critically ill patients with cancer and acute renal dysfunction.

Table 3. Main Associated Factors of Acute Renal Dysfunction (N = 309)

	No.	%
Ischemia/shock	223	72
Sepsis	195	63
Radiocontrast/nephrotoxins	49	16
Urinary tract obstruction (cancer related)	23	7
Unilateral nephrectomy (cancer)	12	4
Acute tumor lysis syndrome	10	3
Multiple myeloma	9	3
Rhabdomyolysis	3	1
Unknown/other	15	5

NOTE. A patient could have more than one associated condition.

Table 1. Criteria for the Classification of Acute Renal Dysfunction

ARI	ARFS	Severe ARFS
Creat > 1.44 mg/dL and urea > 48 mg/dL and/or UO <800 mL/d or UO < 200 mL/6 h	Creat > 2.88 mg/dL and urea > 96 mg/dL and/or UO <400 mL/d or UO < 100 mL/6 h	Need for renal replacement therapy and either criteria for ARI or ARFS
If acute on chronic renal dysfunction: An increase in creat of 0.72 mg/dL or in urea of 24 mg/dL and/or <800/d or UO < 200 mL/6 h	*If acute on chronic renal dysfunction:* An increase in creat of 1.44 mg/dL or in urea of 48 mg/dL and/or UO 400 mL/d or UO < 100 mL/6 h	*If acute on chronic renal dysfunction:* Need for renal replacement therapy and either criteria for acute on chronic renal dysfunction for ARI or ARFS

Abbreviations: ARI, acute renal injury; ARFS, acute renal failure syndrome; creat, serum creatinine concentration; urea, serum urea concentration; UO, urine output.

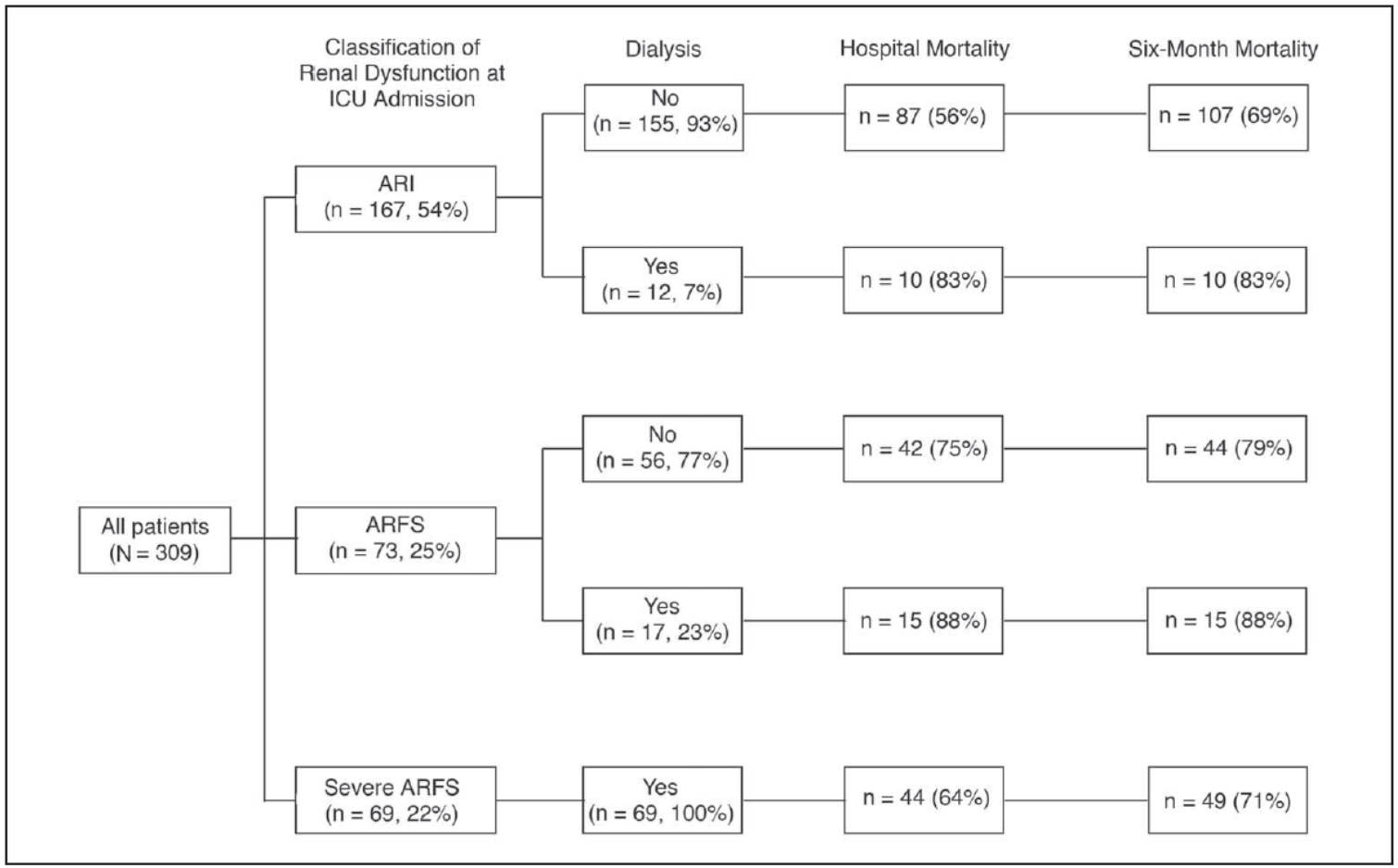

Fig 1. Hospital and 6-month mortality rates according to the initial classification of acute renal dysfunction and temporal indication of dialysis. ICU, intensive care unit; ARI, acute renal injury; ARFS, acute renal failure syndrome.

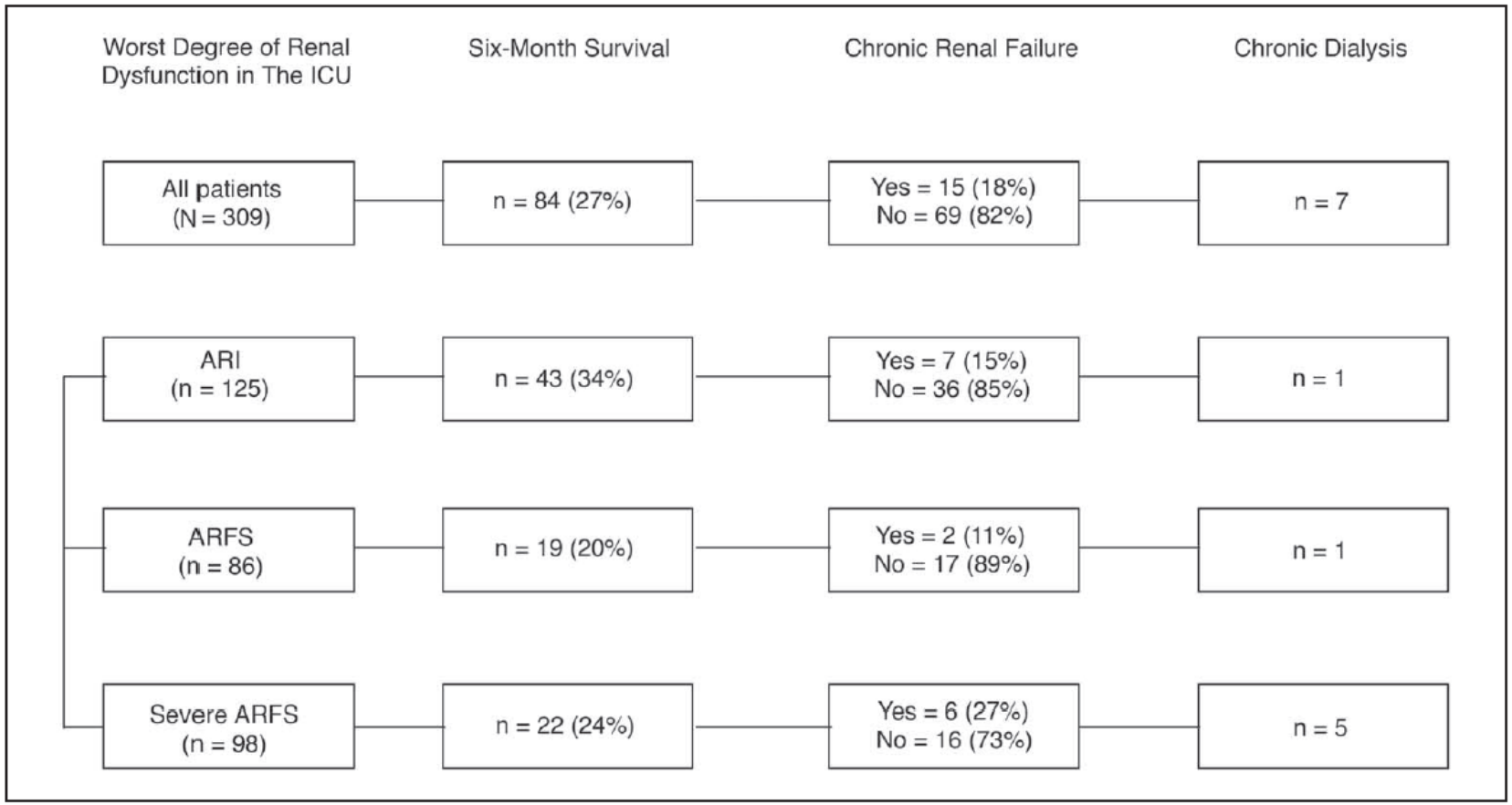

Fig 2. Renal function at 6-months according to the worst classification of acute renal dysfunction during intensive care unit (ICU) stay. ARI, acute renal injury; ARFS, acute renal failure syndrome.

Conclusions

- Les principaux facteurs pronostiques s'avèrent être le nombre d'insuffisances organiques et le délai entre l'admission à l'USI et le début de la dialyse.
- Les caractéristiques du cancer sous-jacent ne sont pas un facteur indépendant, ni le fait d'être atteint d'un cancer.
- La plupart des patients rescapés récupèrent une fonction rénale normale et peu passent en dialyse chronique.

Sous-groupes

Deux sous-groupes ont été identifiés avec des études spécifiques :

1) patients atteints de myélome multiple pour lequel des études randomisées évaluent le bénéfice du traitement extra-rénal des chaînes légères dans les néphropathies myélomateuses cylindriques (« cast nephropathy »)
2) patients à haut risque de syndrome de lyse tumorale

Néphropathie à chaînes légères(myélome multiple)

Deux techniques d'épuration extra-rénale ont été évaluées dans des études de bas niveau de preuve avec un petit échantillon. Ces études suggèrent que les échanges plasmatiques et les membranes de très haute perméabilité ne doivent pas être utilisés dans le seul but de traiter la néphropathie à chaînes légères

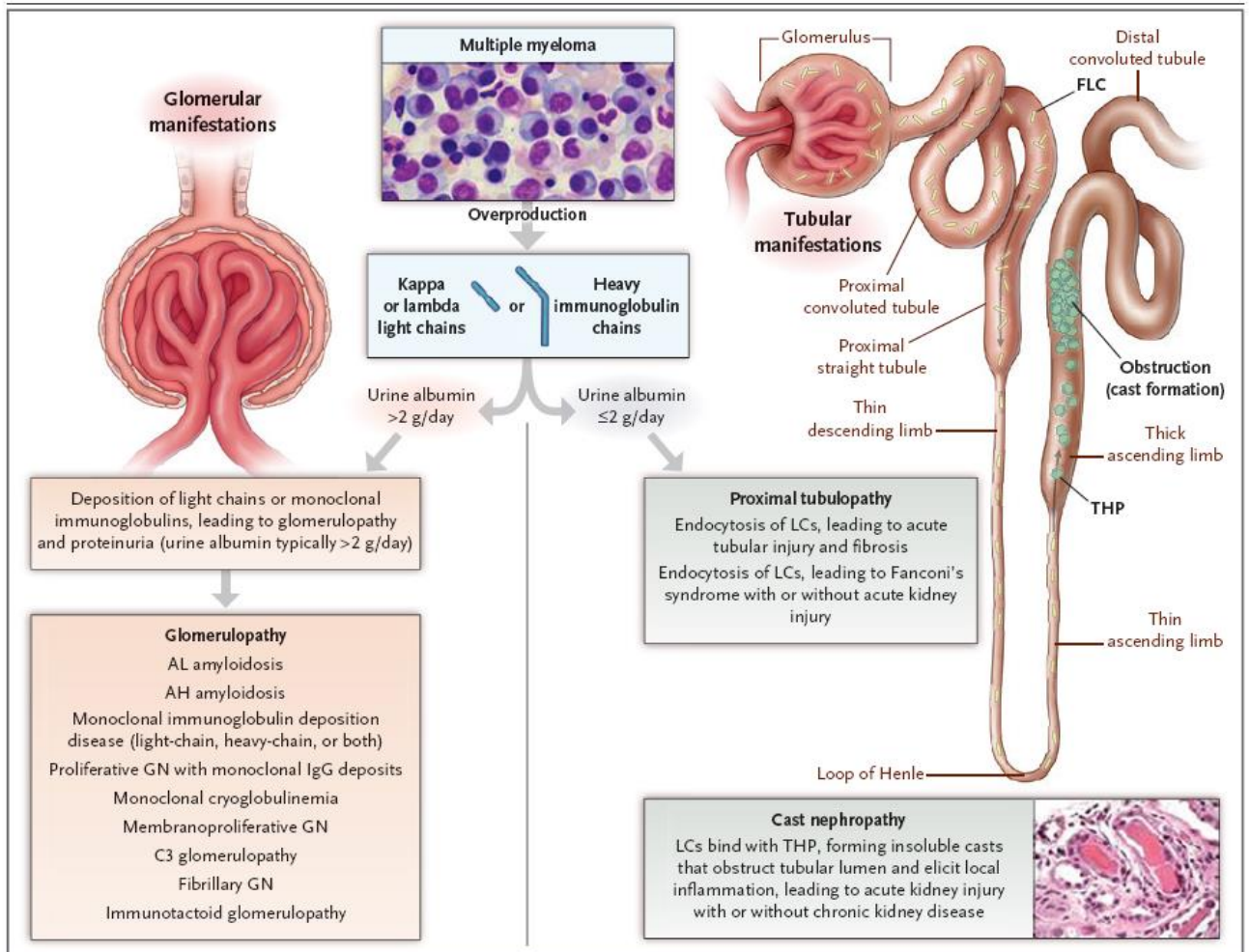

Figure 1. Diagnostic Approach to Patients Presenting with Acute Kidney Injury and Suspected Myeloma.

In patients with multiple myeloma, various glomerular and tubular manifestations can develop. Either isolated light (kappa or lambda) or heavy immunoglobulin chains can lead to injury. Patients with urine albumin levels higher than 2 g per day usually have one of a variety of glomerular lesions, whereas patients with lower urine albumin levels usually have a proximal tubulopathy or cast nephropathy. The stains are Wright–Giemsa (multiple myeloma) and hematoxylin and eosin (cast nephropathy). AH denotes amyloid heavy chain, AL amyloid light chain, FLC free light chain, GN glomerulonephritis, LC light chain, and THP Tamm–Horsfall protein.

N Engl J Med 2017;376:1770-81.
DOI: 10.1056/NEJMra1613984

Myélome multiple

References	Type of study	Uni/Multi	BMT	Type of dialysis	Reason for dialysis	ARF Aetiology	Dialysis location
GERTH et al, 2016 [326]	R	Uni	No	High cut off haemodialysis	NéCy	NéCy	Not specified
HEYNE et al, 2012 [327]	R	Uni	No	High-cut-off haemodialysis	NéCy	NéCy	Not specified
HUTCHISON et al, 2009 [328]	P non-randomised	Uni	No	High-cut-off haemodialysis	NéCy	NéCy	Nephrology
HUTCHISON et al, 2007 [329]	P non-randomised	Uni	No	High-cut-off haemodialysis	NéCy	NéCy	Not specified
HUTCHISON et al, 2012 [330]	P non-randomised	Multi	No	High-cut-off haemodialysis	NéCy	NéCy	Not specified
JOSEPH et al, 2018 [63]	R	Uni	Yes	Intermittent HF + CVVHD	Mixte	Mixte	ICU
KATAGIRI et al, 2011 [331]	R	Uni	No	Intermittent HF	Not specified	Not specified	Not specified
KHALAFALLAH et al, 2013 [61]	P non-randomised	Uni	No	High-cut-off haemodialysis	Not specified	NéCy	Not specified
RODRIGUES et al, 2014 [332]	R	Uni	No	Intermittent HF	Not specified	NéCy	Nephrology
ROUSSEAU-GAGNON et al, 2015 [62]	P non-randomised	Uni	No	Intermittent HF	Anuria	NéCy	Nephrology
SAEZ et al, 2017 [333]	P non-randomised	Uni	Not specified	High-cut-off haemodialysis	NéCy	NéCy	Nephrology
SENS et al, 2017 [334]	R	Uni	Auto	Intermittent HF	NéCy	NéCy	Not specified
ZUCCHELLI et al, 1988 [335]	P randomised	Uni	Not specified	Intermittent HF + Peritoneal	Not specified	NéCy	Not specified

Résultats

References	N patients	Dialysis independence rate	Chronic dialysis rate	Prognostic factors for dialysis independence (Univariate)	Remarks
GERTH et al, 2016 [326]	59	64.3% vs 29.4%	-	-	High cut off haemodialysis versus high flow intermittent
HEYNE et al, 2012 [327]	19	73.7%	17.6%	Duration of ARF before dialysis (multivariate)	
HUTCHISON et al, 2009 [328]	19	73.7%	26.3%	-	
HUTCHISON et al, 2007 [329]	5	60%	40%	-	
HUTCHISON et al, 2012 [330]	67	63%	-	Diminution FLC et delays for HCO	
JOSEPH et al, 2018 [63]	50	46%	20%	High dose chemotherapy, proteinuria (pejorative factors)	
KATAGIRI et al, 2011 [331]	32	62,5%	-	Calcium, beta 2 microglobulin	
KHALAFALLAH et al, 2013 [61]	4	75%	25%	-	
RODRIGUES et al, 2014 [332]	57	18.9%	81.1%	Low Beta 2 microglobulin	Prognostic factors for survival after hospital discharge in multivariate analysis: no dialysis, low C-reactive protein, young age
ROUSSEAU-GAGNON et al, 2015 [62]	16	50%	11.1%	-	
SAEZ et al, 2017 [333]	8	75%	25%	-	
SENS et al, 2017 [334]	17	70.6%	-	Diminution FLC, haematological response	

JAMA | Original Investigation

Effect of High-Cutoff Hemodialysis vs Conventional Hemodialysis on Hemodialysis Independence Among Patients With Myeloma Cast Nephropathy
A Randomized Clinical Trial

Frank Bridoux, MD, PhD; Pierre-Louis Carron, MD; Brigitte Pegourie, MD; Eric Alamartine, MD, PhD; Karine Augeul-Meunier, MD; Alexandre Karras, MD, PhD; Bertrand Joly, MD; Marie-Noëlle Peraldi, MD, PhD; Bertrand Arnulf, MD, PhD; Cécile Vigneau, MD, PhD; Thierry Lamy, MD, PhD; Alain Wynckel, MD; Brigitte Kolb, MD; Bruno Royer, MD; Nolwenn Rabot, MD; Lotfi Benboubker, MD; Christian Combe, MD, PhD; Arnaud Jaccard, MD, PhD; Bruno Moulin, MD, PhD; Bertrand Knebelmann, MD, PhD; Sylvie Chevret, MD, PhD; Jean-Paul Fermand, MD; for the MYRE Study Group

IMPORTANCE Cast nephropathy is the main cause of acute kidney injury in multiple myeloma and persistent reduction in kidney function strongly affects prognosis. Strategies to rapidly remove nephrotoxic serum-free light chains combined with novel antimyeloma agents have not been evaluated prospectively.

Editorial page 2085

Supplemental content

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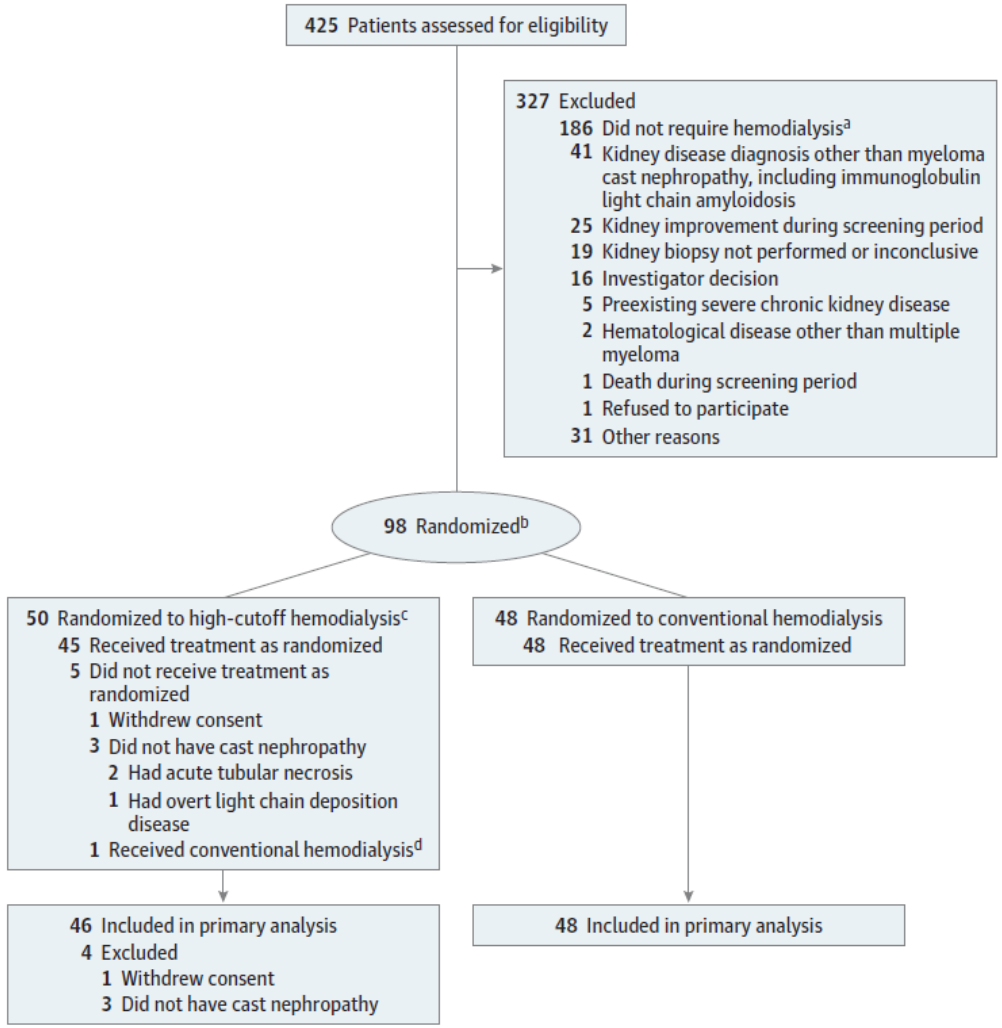
Figure 1. Study Flowchart of High-Cutoff vs Conventional Hemodialysis



[a] Entered another randomized study comparing 2 bortezomib-based chemotherapeutic regimens (bortezomib and dexamethasone vs bortezomib, cyclophosphamide, and dexamethasone) for kidney outcome.

[b] Required treatment with hemodialysis because of the presence of at least 1 of the following: hyperkalemia, metabolic acidosis, fluid overload, or symptoms of uremia.

[c] Allows efficient serum immunoglobulin light chain removal through very large membrane pores.

[d] In accordance with the intention-to-treat principle, this patient was included in the analysis of the high-cutoff hemodialysis group.

Table 1. Baseline Characteristics

Characteristic	No. (%) of Patients[a]	
	High-Cutoff Hemodialysis (n = 46)	Conventional Hemodialysis (n = 48)
Age, y		
Median (IQR)	68.4 (60.9-74.6)	68.8 (62.2-75.7)
<65	17 (37)	14 (29)
≥65	29 (63)	34 (71)
Male sex	23 (50)	29 (60)
Medical history		
Hypertension	23 (50)	30 (63)
Diabetes	7 (15)	7 (15)
Known monoclonal gammopathy of undetermined significance or indolent multiple myeloma	4 (9)	14 (29)
Time from diagnosis of acute kidney injury to chemotherapy, median (IQR), d	8.0 (5.0-12.0)	9.0 (5.5-13.0)
1 Cycle of chemotherapy before randomization		
Bortezomib, cyclophosphamide, and dexamethasone	1 (2)	1 (2)
Cyclophosphamide, thalidomide, and prednisone	0	1 (2)

Multiple Myeloma		
Light chain isotype		
κ	24 (52)	27 (56)
λ	22 (48)	21 (44)
Secreted monoclonal immunoglobulin		
IgG	11 (24)	16 (33)
IgA	12 (26)	7 (15)
IgD		3 (6)
Light chain only	23 (50)	22 (46)
Serum-free light chain level, median (IQR), mg/L	6590 (3421-12 528)	5230 (3023-14 110)
Bone marrow plasma cells, median (IQR), %	38 (22-56)	31 (15-60)
Hemoglobin, median (IQR), g/dL	8.9 (8.2-9.6)	9.5 (8.7-10.2)
Platelet count, median (IQR), $\times 10^9$/L	186 (157-228)	170 (151-209)
β2 microglobulin, median (IQR), mg/L	20.8 (14.9-28.4)	21.8 (14.6-36.0)
Albumin, median (IQR), g/L	32 (28-35)	34 (29-38)
Lactate dehydrogenase level greater than upper limit of normal	6 (13)	9 (19)
Lytic bone lesions	32 (70)	28 (58)
Cytogenetics, No./total (%)		
Standard risk	23/27 (85)	23/31 (74)
High risk[b]	4/27 (15)	8/31 (26)

Kidney Presentation		
De novo acute kidney injury	43 (93)	40 (83)
Known preexisting chronic kidney disease (estimated glomerular filtration rate ≥30 mL/min/1.73 m^2)[c]	3 (6)	8 (17)
Admission to intensive care unit before randomization	7 (15)	8 (17)
Serum creatinine at randomization, median (IQR), mg/dL	6.4 (5.3-8.1)	7.3 (5.2-9.2)
Proteinuria, median (IQR), g/24 h	2.2 (1.4-4.1)	1.7 (1.1-2.7)
Ratio of urine protein to creatinine, median (IQR), mg/mmoL	418 (296-907)	387 (258-623)
Ratio of urine albumin to protein, median (IQR), %	8.5 (4.0-19.8)	8.5 (4.3-20.3)
No. of precipitating factors of cast nephropathy		
0	21 (46)	25 (52)
1	13 (28)	14 (29)
≥2	12 (26)	9 (19)

Table 1. Baseline Characteristics (continued)

Characteristic	No. (%) of Patients[a]	
	High-Cutoff Hemodialysis (n = 46)	Conventional Hemodialysis (n = 48)
Type of precipitating factor		
Angiotensin-converting enzyme inhibitor or angiotensin receptor antagonist use	2 (4)	2 (4)
Diuretic use	1 (2)	6 (13)
Infection	5 (11)	2 (4)
Hypercalcemia	9 (20)	4 (8)
Dehydration	6 (13)	5 (10)
Nonsteroidal anti-inflammatory drug use	18 (39)	15 (31)
Kidney Pathology		
Severe adverse event (bleeding) after biopsy	1 (2)	1 (2)
Typical myeloma casts	46 (100)	46 (96)
Probable cast nephropathy[d]	0	2 (4)
Concomitant light chain–related kidney disease	6 (13)	6 (13)
Light chain deposition disease[e]	4 (9)	6 (13)
Light chain proximal tubulopathy	2 (4)	0

Abbreviation: IQR, interquartile range.

SI conversion factor: To convert creatinine to µmol/L, multiply by 88.4.

[a] Unless otherwise indicated.

[b] Presence of t(4;14), Del17p, or both.

[c] An estimated glomerular filtration rate of less than 30 mL/min/1.73 m^2 at the time of randomization was an exclusion criterion.

[d] In 2 cases with inadequate biopsy samples, the diagnosis was made using indirect lesions (eg, tubular lumen dilatation in the absence of any other cause of AKI).

[e] By immunofluorescence only. Overt disease with typical glomerular lesions was an exclusion criterion.

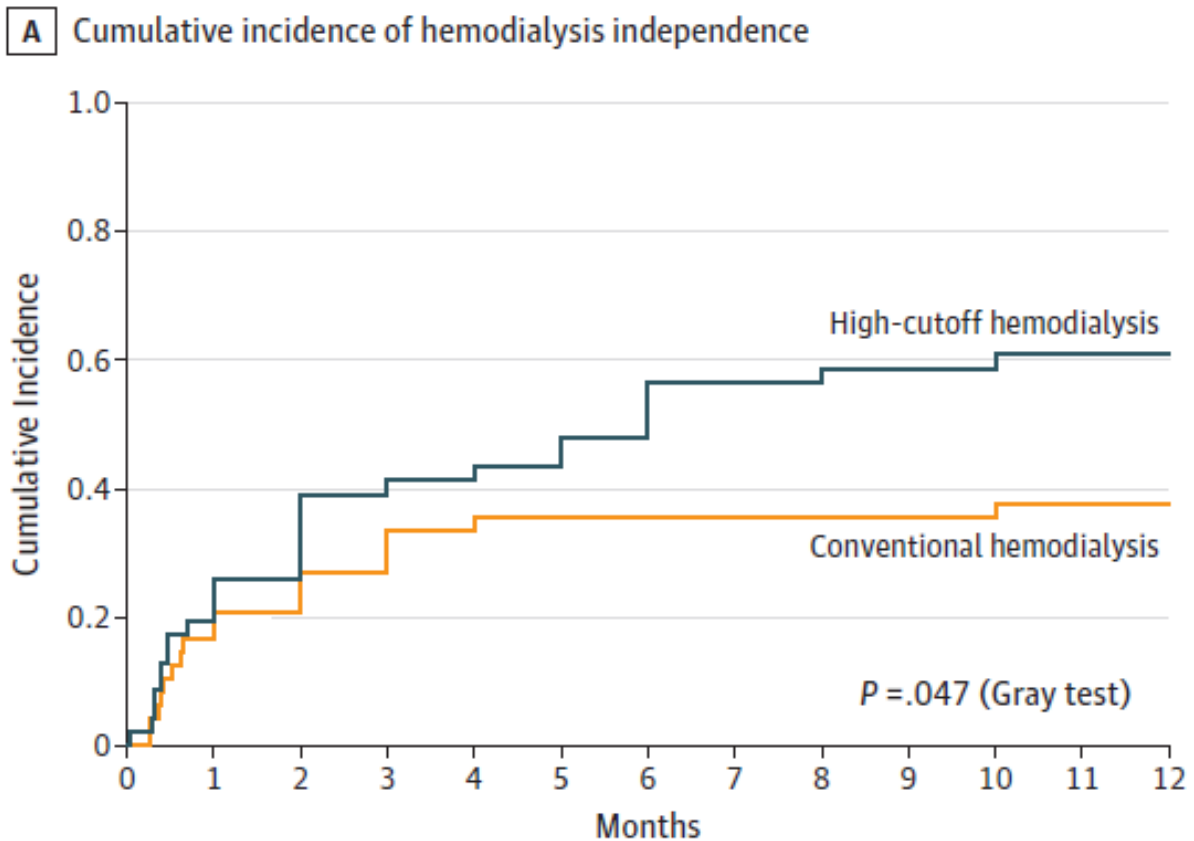
Table 2. Hematologic and Kidney Responses

	No. (%) of Patients[a]			
	High-Cutoff Hemodialysis (n = 46)	Conventional Hemodialysis (n = 48)	Between-Group Difference (95% CI), %	*P* Value
Primary Outcome				
Cumulative hemodialysis independence within 3 mo	19 (41.3)	16 (33.3)	8.0 (−12.0 to 27.9)	.42
Secondary Outcomes				
Cumulative hemodialysis independence within 6 mo	26 (56.5)	17 (35.4)	21.1 (0.9 to 41.3)	.04
Cumulative hemodialysis independence within 12 mo	28 (60.9)	18 (37.5)	23.4 (3.2 to 43.5)	.02
Time to hemodialysis independence, median (IQR), mo	2.0 (0.4 to 5.7)	1.0 (0.4 to 3.0)		.26
Alive without hemodialysis at 12 mo, No./total (%)	24/37 (64.9)	17/38 (44.7)	20.2 (−2.6 to 42.9)	.15
Hematologic response after first chemotherapy cycle				
Reduction in serum-free light chain, median (IQR), %	89 (61 to 99)	71 (22 to 91)		.02
Serum-free light chain level <500 mg/L	20 (43.5)	15 (31.2)	12.3 (−7.7 to 32.1)	.29
Hematologic response at 3 mo				
Overall[b]	41 (89.1)	30 (62.5)	26.6 (9.8 to 43.4)	.003
Very good partial or complete	28 (60.9)	21 (43.7)	17.2 (−3.3 to 37.5)	.22
Hematologic response at 6 mo				
Overall[b]	36 (78.3)	29 (60.4)	17.9 (−0.8 to 36.5)	.06
Very good partial or complete	32 (69.6)	23 (47.9)	21.7 (1.8 to 41.5)	.03
Serum-Free Light Chain Reduction With Hemodialysis				
Reduction after first hemodialysis session, median (IQR), %				
Overall	68 (60 to 79)	31 (9 to 49)		<.001
κ Light chain level	77 (67 to 86)	35 (19 to 48)		<.001
λ Light chain level	63 (52 to 72)	18 (6 to 56)		<.001
Reduction after third hemodialysis session, median (IQR), %				
Overall	72 (64 to 80)	34 (16 to 57)		<.001

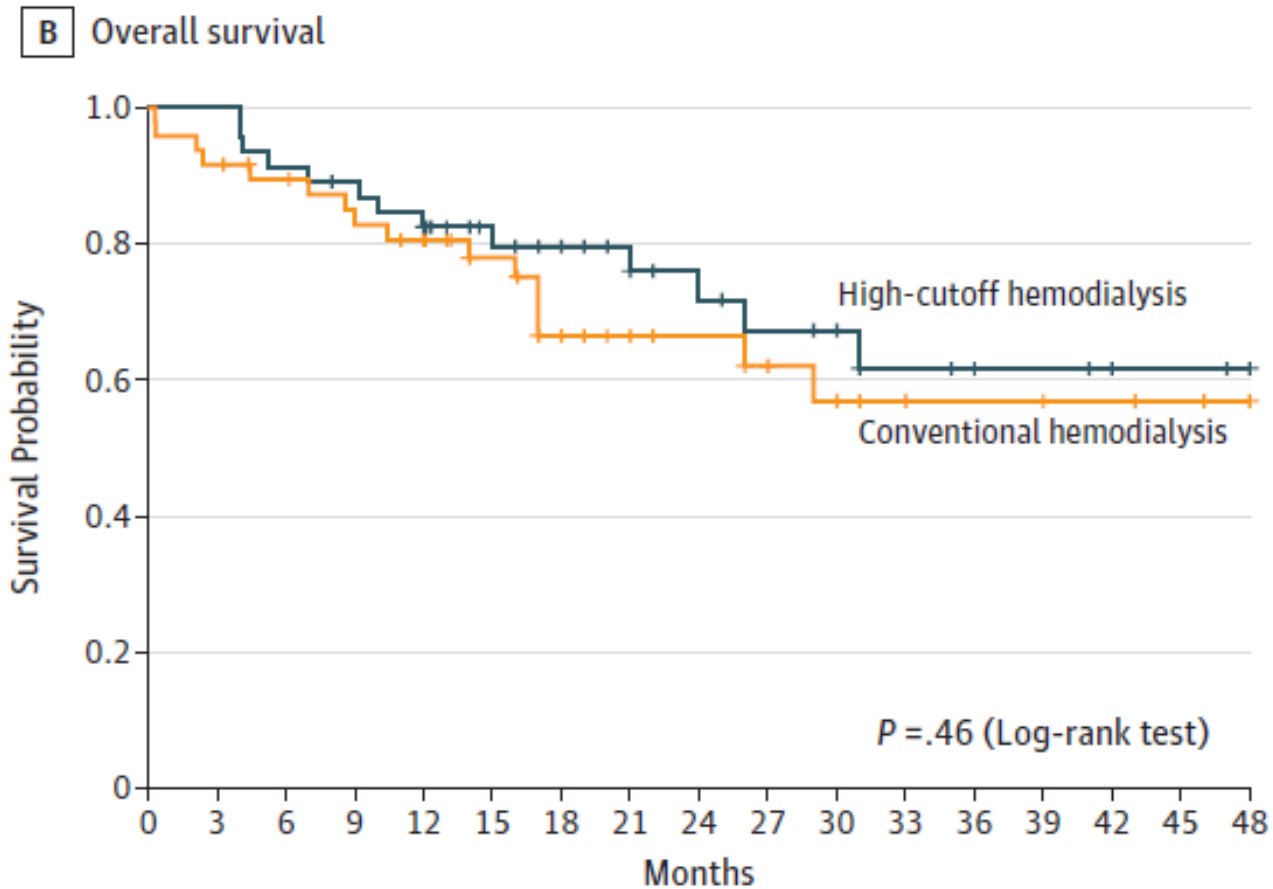
Abbreviation: IQR, interquartile range.

[a] Unless otherwise indicated.

[b] Indicates partial response, very good partial response, and complete response.



No. at risk				
High-cutoff hemodialysis	46	28	22	14
Conventional hemodialysis	48	31	26	21



No. at risk

High-cutoff hemodialysis	46	46	42	40	38	29	25	22	18	15	14	10	9	8	7	6	5
Conventional hemodialysis	48	44	41	38	35	28	22	17	15	13	11	8	7	7	6	5	4

High cutoff versus high-flux haemodialysis for myeloma cast nephropathy in patients receiving bortezomib-based chemotherapy (EuLITE): a phase 2 randomised controlled trial

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https://www.thelancet.com/journals/lanhae/home
https://doi.org/10.1016/S2352-3026(19)30014-6 (11 March 2019)

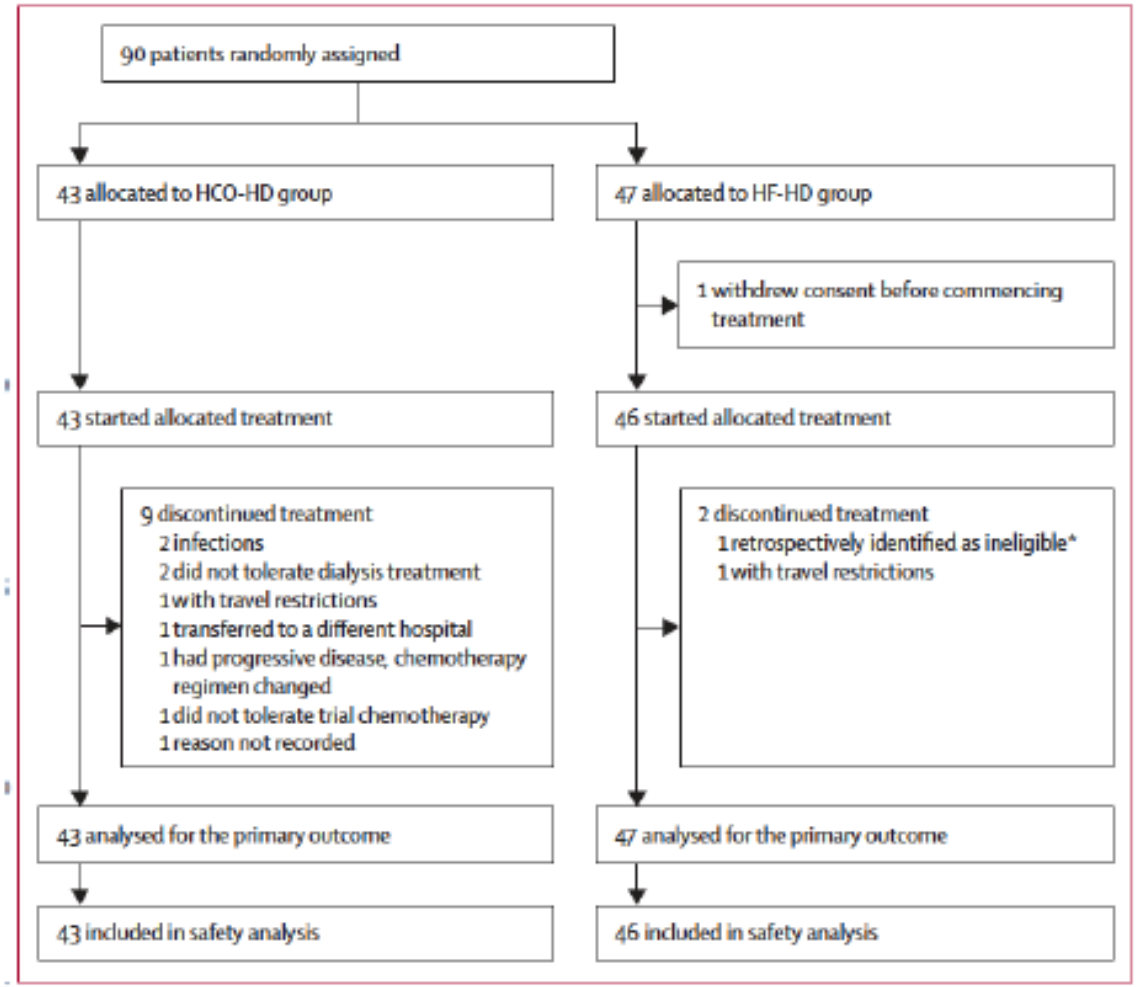


Figure 1: Trial profile

HCO-HD=high cutoff haemodialysis. HF-HD=high-flux haemodialysis. *Identified at day 6 of treatment.

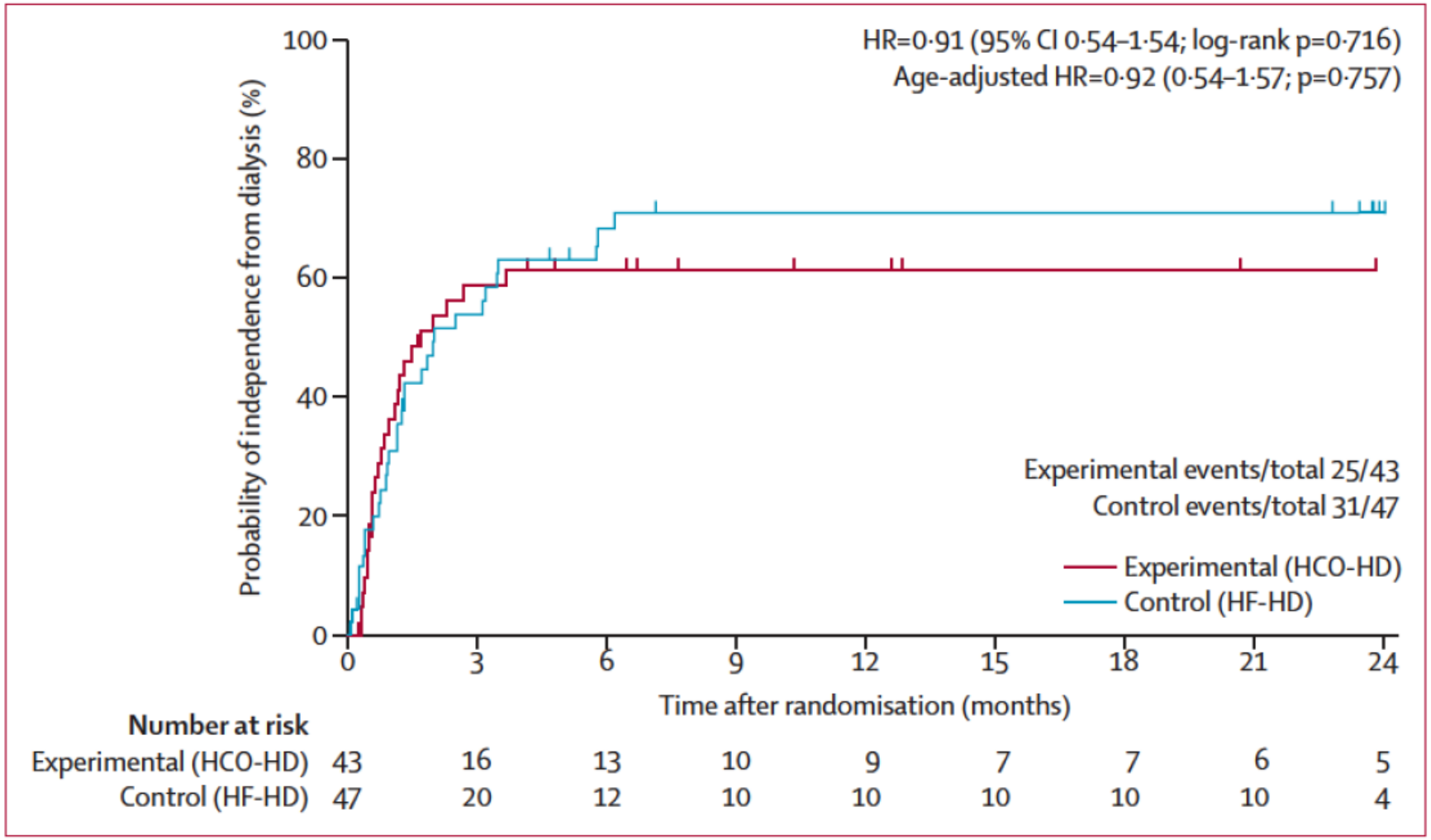


Figure 3: **Reverse Kaplan-Meier graph of time to independence from dialysis by treatment group**
HCO-HD=high cutoff haemodialysis. HF-HD=high-flux haemodialysis. HR=hazard ratio.

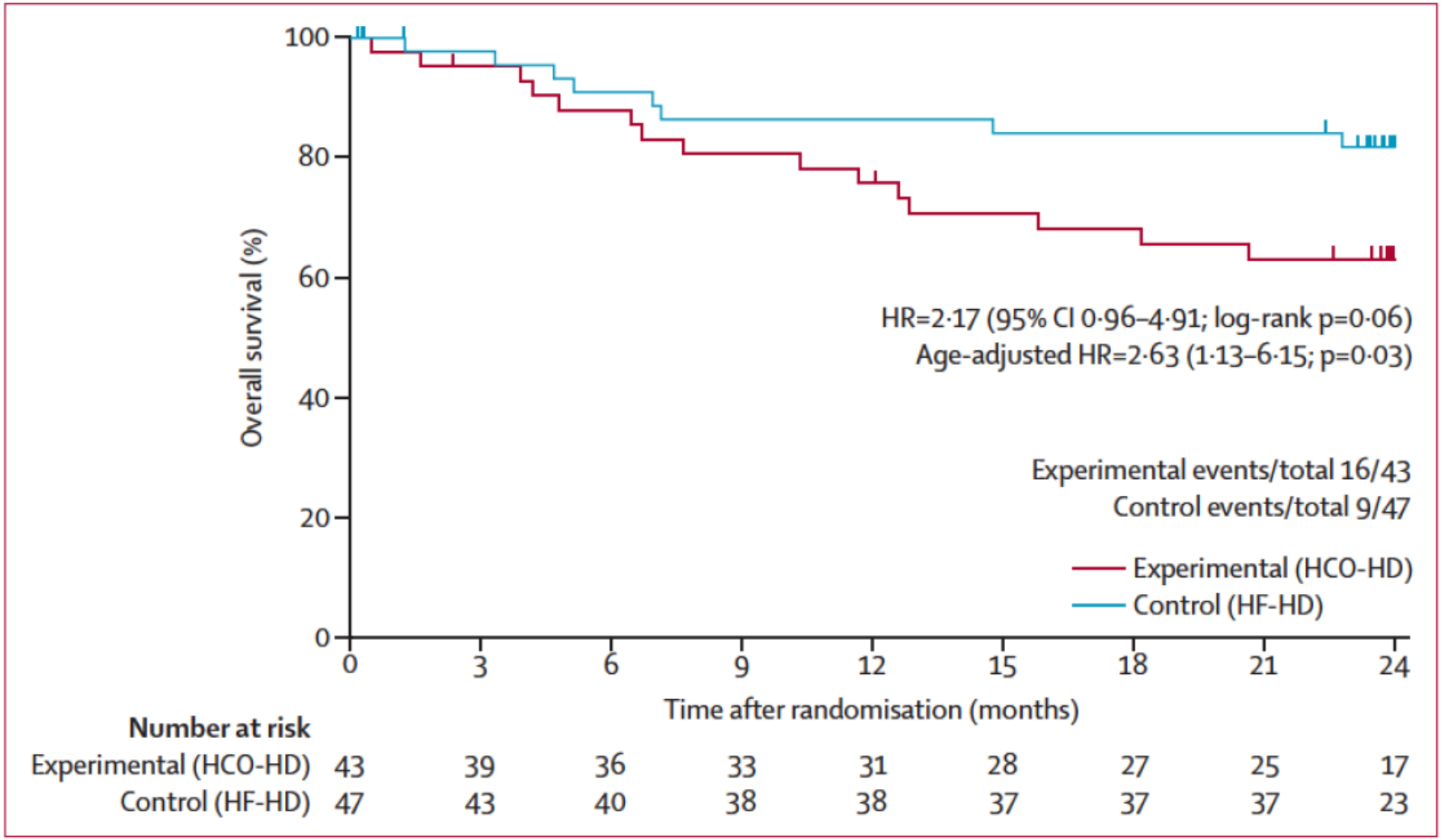


Figure 4: **Kaplan-Meier graph of overall survival by treatment group**
HCO-HD=high cutoff haemodialysis. HF-HD=high-flux haemodialysis. HR=hazard ratio.

Syndrome de lyse tumorale

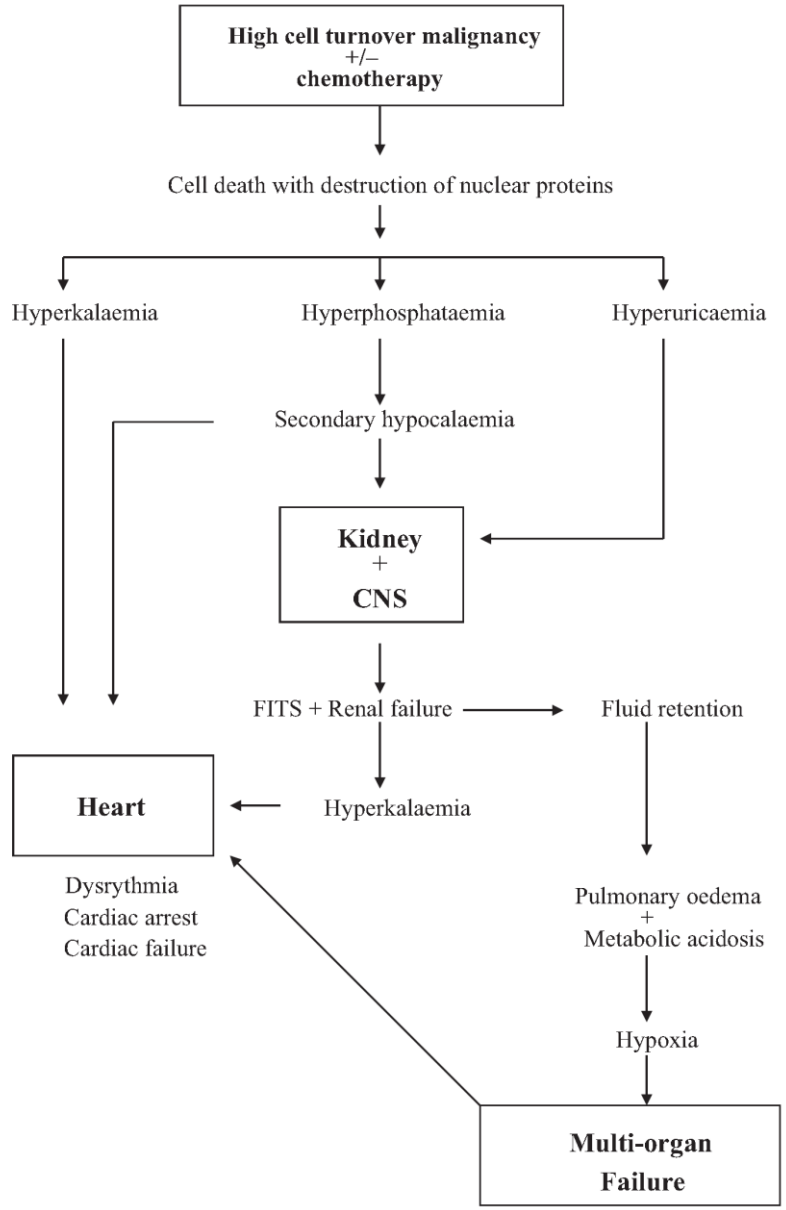
Même si la rasburicase décompose rapidement l'acide urique sérique et est efficace pour prévenir et traiter l'hyperuricémie et le syndrome de lyse tumorale, ces patients présentent un risque élevé de développer une insuffisance rénale aiguë et un risque élevé de décès une fois l'insuffisance rénale aiguë apparue. De plus, les patients atteints de tumeurs malignes de haut grade (leucémie aiguë myéloïde et lymphoblastique et lymphome de haut grade) développant une insuffisance rénale aiguë présentent un risque accru d'échec de l'induction.

Tableau

- hyperkaliémie
- hyperuricémie
- hyperphosphatémie avec hypocalcémie
- augmentation du taux des LDH

risques:

- précipitation de cristaux (urates, phosphates de calcium)
- insuffisance rénale aiguë
- néphrocalcinose
- lithiase urinaire
- troubles de la conduction, arrêt cardiaque


High cell turnover malignancy
+/–
chemotherapy
Cell death with destruction of nuclear proteins
Hyperkalaemia
Hyperphosphataemia
Hyperuricaemia
Secondary hypocalaemia
Kidney
+
CNS
FITS + Renal failure
Fluid retention
Heart
Hyperkalaemia
Dysrythmia
Cardiac arrest
Cardiac failure
Pulmonary oedema
+
Metabolic acidosis
Hypoxia
Multi-organ
Failure

Autres complications de la lyse tumorale aiguë

- troubles de l'hémostase secondaire à la libération d'activités procoagulantes (CIVD) ou protéolytiques (fibrinolyse primitive)
- atteintes rénales tubulaires et glomérulaires secondaires au taux élevé de lysozyme
- pneumopathies alvéolaires aiguës secondaires à la lyse blastique in situ
- perforation d'organes creux siège d'une infiltration tumorale massive

Facteurs déclenchants

dans un contexte de cancer très sensible

a) lyse spontanée : anoxie, nécrose

b) traitement :

- chimiothérapie
- corticothérapie
- radiothérapie

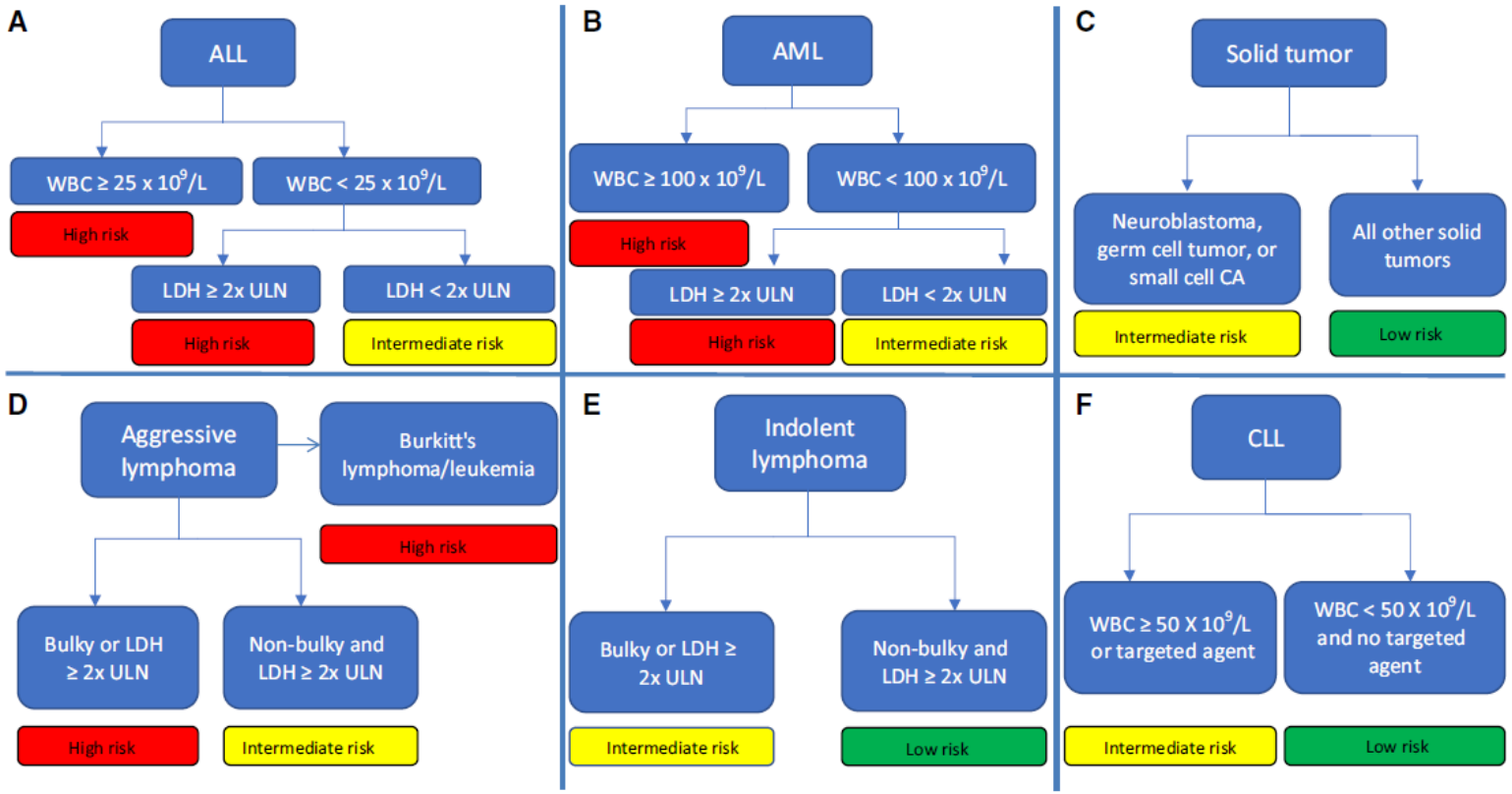


Fig 1. Risk stratification of TLS by tumour type and disease burden (adapted from Cairo *et al.*, 2010).(A) Acute lymphoblastic leukemia (B) Acute myeloid leukemia (C) Solid tumor (D) Aggressive lymphoma (E) Indolent lymphoma (F) Chronic lymphocytic leukemia. Chronic myeloid leukemia and multiple myeloma are very rarely associated with tumor lysis syndrome and thus not included.

Traitement

- à instaurer si possible préventivement
- surveillance (2 à 4 x/j au moins) : K, P, Ca, ac. urique, urée, créatinine, pH artériel, LDH dans le sang

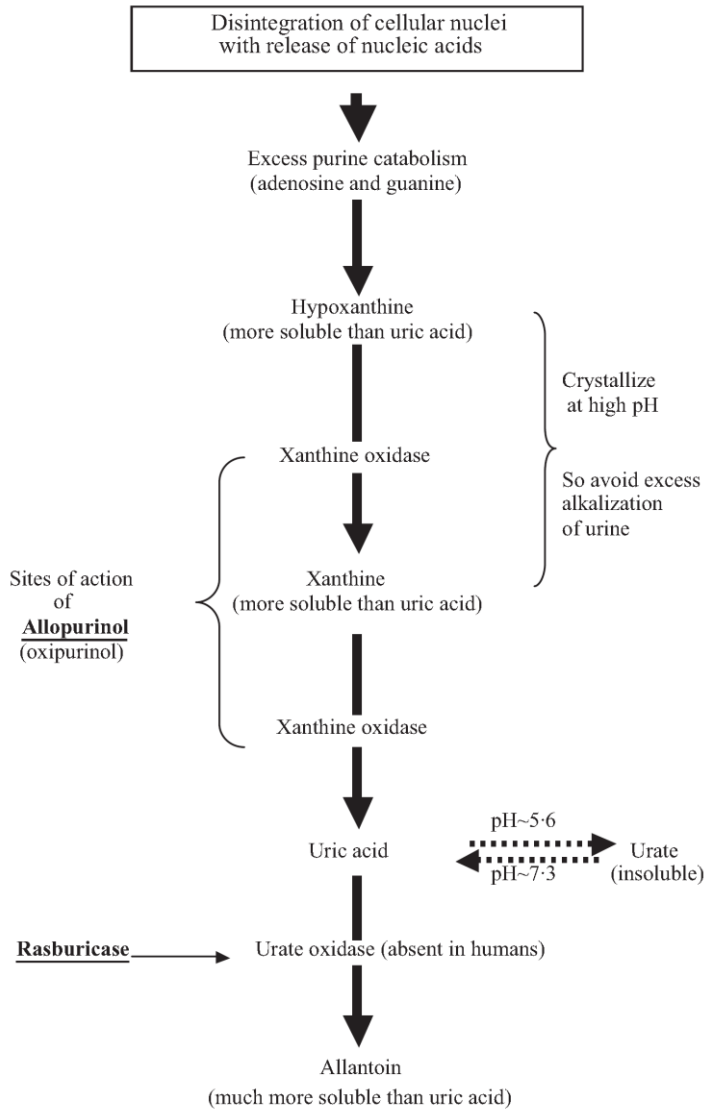


Fig 2. Mechanisms of action of xanthine oxidase inhibitors (allopurinol) and exogenous urate oxidases (rasburicase).

1. Combattre l'hyperuricémie : phase initiale

- hyperdiurèse sodée (NaCl 0,9 %)

  diurèse > 2,5 l /m²/24 h

  éviter l'alcalose systémique (**ne pas alcaliniser**)

- hypouricémiant : **urate-oxydase** (rasburicase ou Fasturtec^{R} amp à 1,5 et à 7,5 mg)

  - effets secondaires potentiels: réactions d'hypersensibilité
  - 0,20 mg/kg une fois par jour iv
  - en Belgique: remboursé par la sécurité sociale uniquement en cas d'hémopathie maligne

2. Traitement cytotoxique (antitumoral)

à débuter au mieux après contrôle de la situation métabolique initiale et obtention d'une hyperdiurèse correcte

3. Combattre l'hyperphosphaturie et l'hyperkaliémie

en fin de traitement cytotoxique

- maintenir l'hyperdiurèse sodée, en ayant éventuellement recours au furosémide
- en cas d'hyperkaliémie (> 5 mEq/L) : Kayexalate 15 g p.o. toutes les 6 à 8 h

4. Epuration extrarénale

indications :

- rétention hydrosodée
- hyperphosphatémie non rapidement réversible : produit [P x Ca] < 4,6 (en mmol/l)
- acidose
- hyperkaliémie
- insuffisance rénale aiguë
- hypocalcémie symptomatique

(la prise en charge sera précoce, avant l'apparition de l'aplasie chimio-induite)

Recommandations

- Il est probablement conseillé de recommander une stratégie d'EER chez les patients cancéreux similaire à la population générale des soins intensifs. La modalité de type d'EER (aiguë intermittente vs continue ou précoce vs tardive) doit être adaptée à l'expertise locale (avis d'expert, faible recommandation).
- Il est probablement nécessaire d'admettre les patients à haut risque de syndrome de lyse tumorale en réanimation (avis d'expert, faible recommandation).
- Une collaboration étroite entre l'onco-hématologue et le réanimateur est essentielle pour une prise en charge optimale du syndrome de lyse tumorale et de la malignité sous-jacente (avis d'expert, recommandation forte).

- L'utilisation d'une stratégie d'EER précoce n'est pas validée chez le patient présentant un syndrome de lyse tumorale mais est étayée par des arguments physiopathologiques indirects (épuration des phosphates considérée comme une cause dans le développement de l'insuffisance rénale aiguë), par la gravité et ses conséquences. L'EER peut donc être proposée comme technique de contrôle métabolique chez les patients atteints du syndrome de lyse tumorale qui ne répondent pas à un traitement médical optimal (avis d'expert, recommandation forte).
- En cas d'hémodialyse intermittente, un risque de rebond du syndrome de lyse tumorale avec anomalies métaboliques a été rapporté dans des séries de cas. En cas d'hémodialyse intermittente, il est préférable d'initier des séances d'hémodialyse intermittente répétées itératives quotidiennes (avis d'expert, recommandation forte).
- L'échange de plasma et les membranes à seuil élevé ne doivent pas être utilisés dans le seul but de traiter la néphropathie à chaînes légères (GRADE B, forte recommandation)