



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

Les Diurétiques en Réanimation: PRO

Dr Raphaël CINOTTI

Congrès SFAR Jeudi 23 Septembre



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

Conflits d'intérêts

- Néant



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

Indications

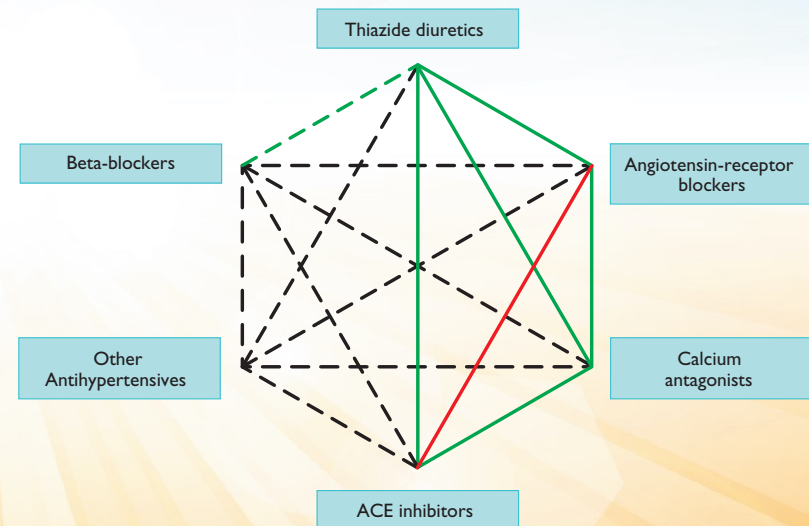
- Insuffisance cardiaque aiguë et chronique
- Œdème pulmonaire cardiogénique
- Hypertension artérielle
- Insuffisance rénale aiguë et chronique
- Divers: hyperkaliémie, hypercalcémie

Autres contextes?

Cardiologie - HTA

Treatment strategies and choice of drugs

Recommendations	Class ^a	Level ^b	Ref. ^c
Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other.	I	A	284, 332



ACE = angiotensin-converting enzyme.

Autres contextes?

Cardiologie – Insuffisance Cardiaque Aiguë et chronique

Recommendations for the treatment of hypertension in patients with symptomatic HF (NYHA functional class II–IV) and LV systolic dysfunction

Recommendation	Class	Level	Ref.
Class I Diuretics are recommended for HF patients with NYHA functional class II–IV, symptomatic HF, and LV systolic dysfunction. (Level of evidence: moderate to high)	A	I	107, 108 (1)
Class IIa A diuretic should be used if the patient is treated with a diuretic already, and adding a loop diuretic is recommended. (Level of evidence: moderate to high)	A	I	107, 108 (1)
Class IIb Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	II	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)
Class III Diuretics are recommended when loop diuretic therapy is not sufficient to control symptoms. (Level of evidence: moderate to high)	A	III	107, 108 (1)

The effects of diuretics on mortality and morbidity have not been studied in patients with HF, unlike ACE inhibitors, beta-blockers, and MRAs (and other treatments). However, diuretics relieve dyspnoea and oedema and are recommended for this reason in patients with signs and symptoms of congestion, irrespective of EF.

Table 16 Doses of diuretics commonly used to treat heart failure (with and without a preserved ejection fraction, chronic and acute)

Diuretics	Initial dose (mg)	Usual daily dose (mg)		
Loop diuretics^a				
Furosemide	20–40	40–240		
Bumetanide	0.5–1.0	1–5		
Torsemide	5–10	10–20		
Thiazides^b				
Bendroflumethiazide	2.5	2.5–10		
Hydrochlorothiazide	25	12.5–100		
Metolazone	2.5	2.5–10		
Indapamide ^c	2.5	2.5–5		
Potassium-sparing diuretics^d				
	+ACEi/ ARB	-ACEi/ ARB	+ACEi/ ARB	-ACEi/ ARB
Spirolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

Autres contextes?

Cardiologie – Insuffisance Cardiaque Aiguë et chronique

Table 16 Doses of diuretics commonly used to treat heart failure (with and without a preserved ejection fraction, chronic and acute)

Diuretics	Initial dose (mg)	Usual daily dose (mg)		
Loop diuretics*				
Furosemide	20–40	40–240		
Bumetanide	0.5–1.0	1–5		
Torsemide	5–10	10–20		
Thiazides*				
Bendroflumethiazide	2.5	2.5–10		
Hydrochlorothiazide	25	12.5–100		
Metolazone	2.5	2.5–10		
Indapamide [†]	2.5	2.5–5		
Potassium-sparing diuretics[‡]				
	+ACEI/ ARB	-ACEI/ ARB	+ACEI/ ARB	-ACEI/ ARB
Spirinolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

The effects of diuretics on mortality and morbidity have not been studied in patients with HF, unlike ACE inhibitors, beta-blockers, and MRAs (and other treatments). However, diuretics relieve dyspnoea and oedema and are recommended for this reason in patients with signs and symptoms of congestion, irrespective of EF.

Recommendations for the treatment of hypertension in patients with symptomatic HF (NYHA functional class II–IV) and LV systolic dysfunction

Recommendations	Class ^a	Level ^b	Ref ^c
Step 1			
One or more of an ACE inhibitor (or ARB), beta-blocker, and MRA is recommended as first-, second-, and third-line therapy, respectively, because of their associated benefits (reducing the risk of HF hospitalization and reducing the risk of premature death).	I	A	87, 108–111
Step 2			
A thiazide diuretic (or if the patient is treated with a thiazide diuretic, switching to a loop diuretic) is recommended when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, and MRA.	I	C	–
Step 3			
Amlodipine is recommended when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, MRA, and diuretic.	I	A	188, 189
Hydralazine is recommended when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, MRA, and diuretic.	I	A	114–116
Felodipine should be considered when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, MRA, and diuretic.	IIa	B	204
Moxonidine is NOT recommended because of safety concerns (increased mortality).	III	B	203
Alpha-adrenoceptor antagonists are NOT recommended because of safety concerns (neurohumoral activation, fluid retention, worsening HF).	III	A	202, 206, 207

Autres contextes?

Cardiologie – Insuffisance Cardiaque Aiguë et chronique

Recommendations for the treatment of hypertension in patients with symptomatic HF (NYHA functional class II-IV) and LV systolic dysfunction

Recommendation	Class	Level	Ref.
Diuretics should be used in patients with HF and LV systolic dysfunction to relieve symptoms and reduce morbidity and mortality.	A	I	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100
Diuretics should be used in patients with HF and LV systolic dysfunction to reduce morbidity and mortality.	A	I	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100
Diuretics should be used in patients with HF and LV systolic dysfunction to improve quality of life.	A	I	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100

Table 16 Doses of diuretics commonly used to treat heart failure (with and without a preserved ejection fraction, chronic and acute)

Diuretics	Initial dose (mg)	Usual daily dose (mg)		
Loop diuretics^a				
Furosemide	20–40	40–240		
Bumetanide	0.5–1.0	1–5		
Torsemide	5–10	10–20		
Thiazides^b				
Bendroflumethiazide	2.5	2.5–10		
Hydrochlorothiazide	25	12.5–100		
Metolazone	2.5	2.5–10		
Indapamide ^c	2.5	2.5–5		
Potassium-sparing diuretics^d				
	+ACE/ ARB	-ACE/ ARB	+ACE/ ARB	-ACE/ ARB
Spirolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

The effects of diuretics on mortality and morbidity have not been studied in patients with HF, unlike ACE inhibitors, beta-blockers, and MRAs (and other treatments). However, diuretics relieve dyspnoea and oedema and are recommended for this reason in patients with signs and symptoms of congestion, irrespective of EF.

Autres contextes?

Néphrologie – IRC et IRA

Medication Choices

- 8.1.4-1. Simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended to treat adults with hypertension. (COR III: Harm, LOE A)
- 8.1.6-1. For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs. (COR I, LOE A^{SR})

Diuretics

Recommendations

1. We *recommend* against loop diuretics given solely for the prevention of acute kidney injury (Grade 1B).
2. We *suggest* using diuretics to control or avoid fluid overload in patients that are diuretic-responsive (Grade 2D).



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

En réanimation

Comment utilisez-vous les diurétiques?

- Sevrage VM
- Surcharge hydro-sodée
- Insuffisance rénale oligurique
- Hyperkaliémie

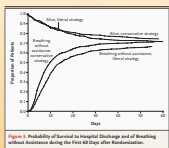
Ventilation mécanique

Table 2. Furosemide Dose, Fluid Intake, Fluid C

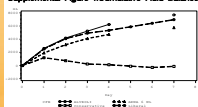
Day	Furosemide	
	Liberal	Conservative
	mg/24 hr (no. of patients)	
1	74.27±7.48 (133)	148.94±8.52 (312)
2	72.46±6.65 (146)	157.35±8.91 (304)
3	65.28±6.49 (140)	166.90±10.01 (269)
4	80.74±10.23 (129)	154.25±10.61 (228)
5	73.06±8.41 (119)	164.71±12.06 (197)
6	58.20±6.68 (106)	158.87±13.45 (165)
7	51.03±4.31 (87)	127.86±11.61 (137)

Table 3. Main Outcome Variables^a

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28 ^b	14.6±0.5	12.1±0.5	<0.001
ICU-free days ^c			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001



Supplemental Figure 1. Cumulative Fluid Balance



Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine ≤5 µg/kg/min); consider correctable causes of shock first	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 µg/kg/min)			
CVP		PAOP ^G			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		Ineffective Circulation Cardiac index <2.5 liters/min/m ² or cold, mottled skin with capillary-refilling time >2 sec	Effective Circulation Cardiac index ≥2.5 liters/min/m ² or absence of criteria for ineffective circulation	Ineffective Circulation Cardiac index <2.5 liters/min/m ² or cold, mottled skin with capillary-refilling time >2 sec	Effective Circulation Cardiac index ≥2.5 liters/min/m ² or absence of criteria for ineffective circulation
Range 1				1 Vasopressor ^F Fluid bolus ^F	3 KVO IV Dobutamine ^A Furosemide ^{B,1,2,4}	7 KVO IV Furosemide ^{B,1,2,4}	11 KVO IV Dobutamine ^A Furosemide ^{B,1,3,4}	15 KVO IV Furosemide ^{B,1,3,4}
>13	>18	>18	>24					
Range 2				4 KVO IV Dobutamine ^A	8 KVO IV Furosemide ^{B,1,2,4}	12 KVO IV Dobutamine ^A	16 KVO IV Furosemide ^{B,1,3,4}	
9–13	15–18	13–18	19–24					
Range 3				2 Fluid bolus ^F Vasopressor ^F	5 Fluid bolus ^C	9 Fluid bolus ^C	13 Fluid bolus ^C	17 Liberal KVO IV
4–8	10–14	8–12	14–18				18 Conservative Furosemide ^{B,1,3,4}	
Range 4				6 Fluid bolus ^C	10 Fluid bolus ^C	14 Fluid bolus ^C	19 Liberal fluid bolus	
<4	<10	<8	<14				20 Conservative KVO IV	

Ventilation mécanique

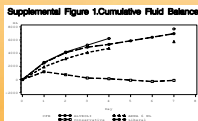
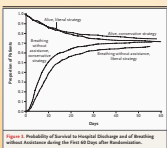
Table 2. Furosemide Dose, Fluid Intake, Fluid C

Day	Furosemide	
	Liberal	Conservative
	<i>mg/24 hr (no. of patients)</i>	
1	74.27±7.48 (133)	148.94±8.52 (312)
2	72.46±6.65 (146)	157.35±8.91 (304)
3	65.28±6.49 (140)	166.90±10.01 (269)
4	80.74±10.23 (129)	154.25±10.61 (228)
5	73.06±8.41 (119)	164.71±12.06 (197)
6	58.20±6.68 (106)	158.87±13.45 (165)
7	51.03±4.31 (87)	127.86±11.61 (137)

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001

Table 3. Main Outcome Variables.*

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001





du 23 au 25
Septembre 2021
PALAIS
DES CONGRÈS
DE PARIS

Ventilation mécanique

Mortalité à 60 jours (%)		Mortalité à 28 jours (%)		Mortalité à 7 jours (%)	
Liberal	Conservative	Liberal	Conservative	Liberal	Conservative
25.5	28.4	25.5	28.4	25.5	28.4

Table 2. Furosemide Dose, Fluid Intake, Fluid C

Day	Furosemide mg/24 hr (no. of patients)	
	Liberal	Conservative
1	74.27±7.48 (133)	148.96±8.52 (312)
2	72.46±6.65 (146)	157.35±8.91 (304)
3	65.28±6.49 (140)	166.90±10.01 (269)
4	80.74±10.23 (129)	154.25±10.61 (228)
5	73.06±8.41 (119)	164.71±12.06 (197)
6	58.20±6.68 (106)	158.87±13.45 (165)
7	51.03±4.31 (87)	127.86±11.61 (137)

Table 3. Main Outcome Variables.^a

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days‡			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001

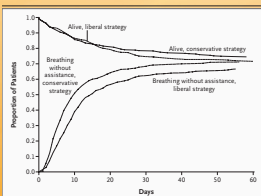
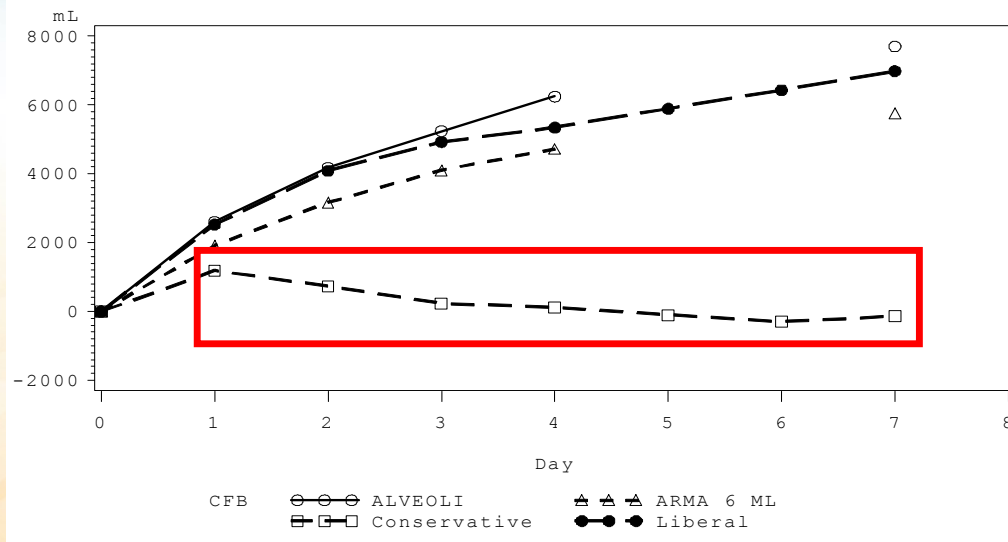


Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

Supplemental Figure 1. Cumulative Fluid Balance

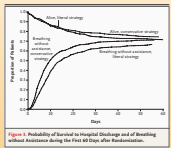


Ventilation mécanique

Outcome	Liberal	Conservative	P Value
Death at 60 days (%)	28.4	25.5	0.30
Ventilator-free days from day 1 to day 28†	12.1±0.5	14.6±0.5	<0.001
ICU-free days‡			
Days 1 to 7	0.6±0.1	0.9±0.1	<0.001
Days 1 to 28	11.2±0.4	13.4±0.4	<0.001

Table 2. Furosemide Dose, Fluid Intake, Fluid C

Day	Furosemide mg/24 hr (no. of patients)	
	Liberal	Conservative
1	74.27±7.48 (133)	148.96±8.52 (312)
2	72.46±6.65 (146)	157.35±8.91 (304)
3	65.28±6.49 (140)	166.90±10.01 (269)
4	80.74±10.23 (129)	154.25±10.61 (228)
5	73.06±8.41 (119)	164.71±12.06 (197)
6	58.20±6.68 (106)	158.87±13.45 (165)
7	51.03±4.31 (87)	127.86±11.61 (137)



Supplemental Figure 1. Cumulative Fluid Balance

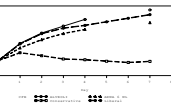


Table 3. Main Outcome Variables.*

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days‡			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001

Ventilation mécanique

Outcome	Liberal	Conservative	P Value
Death at 60 days (%)	28.4	25.5	0.30
Ventilator-free days from day 1 to day 28†	12.1±0.5	14.6±0.5	<0.001
ICU-free days‡	0.6±0.1	0.9±0.1	<0.001
Days 1 to 7	0.6±0.1	0.9±0.1	<0.001
Days 1 to 28	11.2±0.4	13.4±0.4	<0.001

Table 2. Furosemide Dose, Fluid Intake, Fluid C

Day	Liberal mg/24 hr (no. of patients)	Conservative mg/24 hr (no. of patients)
1	74.27±7.48 (133)	148.96±8.52 (312)
2	72.46±6.65 (146)	157.35±8.91 (304)
3	65.28±6.49 (140)	166.90±10.01 (269)
4	80.74±10.23 (129)	154.25±10.61 (228)
5	73.06±8.41 (119)	164.71±12.06 (197)
6	58.20±6.68 (106)	158.87±13.45 (165)
7	51.03±4.31 (87)	127.86±11.61 (137)

Table 3. Main Outcome Variables.*

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days‡	0.9±0.1	0.6±0.1	<0.001
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001

Supplemental Figure 1. Cumulative Fluid Balance

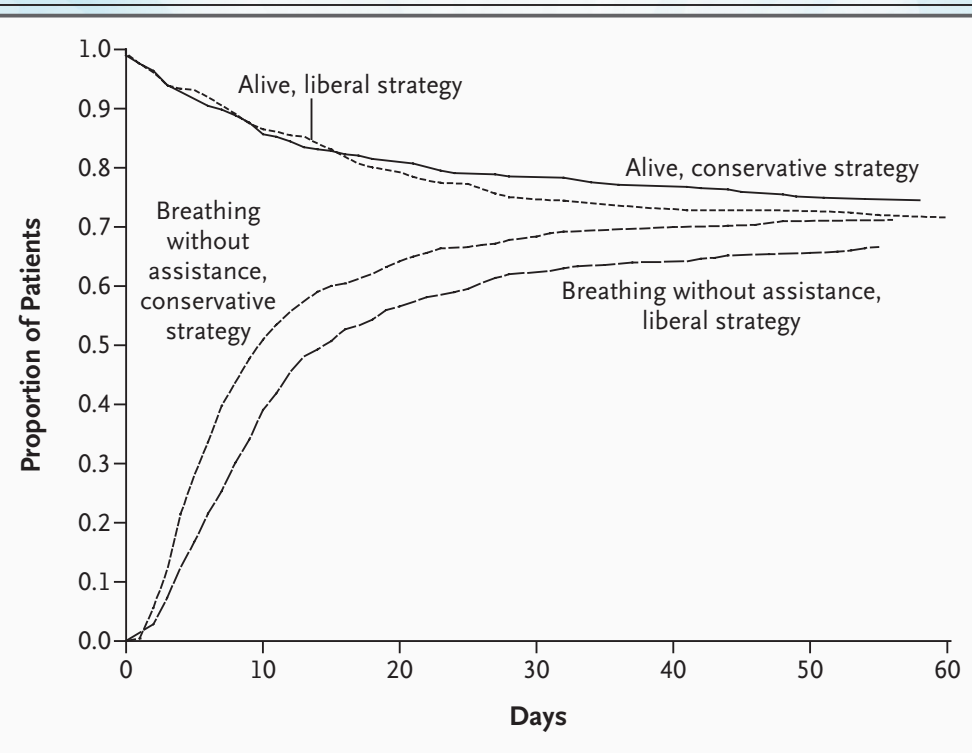
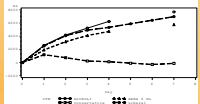


Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

Ventilation mécanique

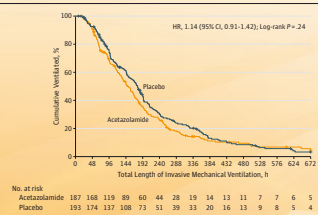
Table 2. Clinical Outcomes and Serious Adverse Events*

Variable	Group, Median (Interquartile Range)		Between-Group Difference (95% CI)	P Value
	Acetazolamide (n = 187)	Placebo (n = 193)		
Primary Outcomes				
Duration of invasive ventilation, h	136.5 (88.7 to 234.7)	163 (86.2 to 242.0)	-16.0 (-36.5 to 4.0)	.17
Secondary Outcomes^b				
Daily				
Serum bicarbonate change, mEq/L	-0.3 (-1.0 to 0.4)	0.3 (-0.2 to 1.3)	-0.8 (-1.2 to -0.5)	<.001
PaCO ₂ change, mm Hg	-0.5 (-2.0 to 0.8)	-0.2 (-1.4 to 1.1)	-0.3 (-0.8 to 0.2)	.25
pH change	0 (-0.01 to 0.02)	0.01 (0 to 0.02)	-0.01 (-0.01 to -0.0)	.008
PaO ₂ /F _{IO₂} change, mm Hg	7.8 (1.5 to 20.5)	3.5 (-5.2 to 11.8)	4.6 (0.8 to 8.0)	.009
Respiratory rate change, cycles/min	0.1 (-0.8 to 1.0)	0.3 (-0.3 to 1.4)	-0.3 (-0.7 to 0.0)	.10
Tidal volume change, mL	4.1 (-7.1 to 28.0)	3.8 (-8.6 to 19.4)	1.3 (-4.2 to 7.5)	.72
Volume-minute change, L/min	0.2 (-0.2 to 0.8)	0.2 (-0.1 to -0.8)	0.0 (-0.2 to 0.2)	.72
Weaning duration, h	18.7 (3.0 to 46.5)	22.0 (3.0 to 44.3)	-0.8 (-4.9 to 1.3)	.36
Spontaneous breathing trials, d	1 (1 to 2)	1 (1 to 2)	0 (0 to 0)	.42
Tracheostomy, median (range), d	0 (0 to 23)	0 (0 to 9)	0 (0 to 0)	.67
Endotracheal intubation, No. (%)	187 (100)	192 (99.5)	0.05 (-0.05 to 1.5)	.99
Use of noninvasive ventilation after extubation, No. (%)	62 (33.1)	72 (37.3)	-4.2 (-13.8 to 5.5)	.39
Successful weaning, No. (%) ^c	118 (74.7)	127 (78.4)	-3.7 (-13.1 to 5.6)	.43

Table 1. Characteristics of the Patients at Baseline

Characteristic	Study Group, Mean (SD)	
	Acetazolamide (n = 187)	Placebo (n = 193)
Age, y	69 (10)	69 (11)
Men, No. (%)	131 (70)	141 (73.1)
SAPS II score ^a	49.4 (13.9)	50 (15.1)
SOFA score ^b	7.2 (3.1)	7.1 (3.2)
BMI	27.2 (8.0)	26.7 (9.1)

Figure 2. Kaplan-Meier Curves for the Cumulative Probabilities of Being Weaned Off Invasive Ventilation



Ventilation mécanique

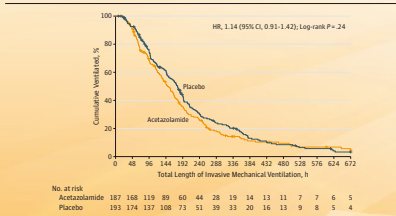
Table 2. Clinical Outcomes and Serious Adverse Events^a

Variable	Group, Median (Interquartile Range)		Between-Group Difference (95% CI)	P Value
	Acetazolamide (n = 187)	Placebo (n = 193)		
Primary Outcome				
Duration of invasive ventilation, h	136.5 (68.7 to 234.7)	163 (86.2 to 242.9)	-16.0 (-36.5 to 4.0)	.17
Secondary Outcomes^b				
Daily				
Serum bicarbonate change, mEq/L	-0.3 (-1.0 to 0.4)	0.3 (-0.2 to 1.3)	-0.8 (-1.2 to -0.5)	<.001
Paco ₂ change, mm Hg	-0.5 (-2.0 to 0.8)	-0.2 (-1.4 to 1)	-0.3 (-0.8 to 0.2)	.25
pH change	0 (-0.01 to 0.02)	0.01 (0 to 0.02)	-0.01 (-0.01 to -0.0)	.008
Pao ₂ :Fio ₂ -ratio change, mm Hg	7.8 (-1.5 to 20.5)	3.5 (-5.2 to 13.9)	4.6 (0.6 to 8.6)	.009
Respiratory rate change, cycle/min	0.1 (-0.8 to 1.0)	0.3 (-0.3 to 1.4)	-0.3 (-0.7 to 0.0)	.10
Tidal volume change, mL	4.1 (-7.1 to 28.0)	3.8 (-8.6 to 19.4)	1.3 (-4.2 to 7.5)	.72
Volume-minute change, L/min	0.2 (-0.2 to 0.8)	0.2 (-0.1 to -0.6)	0.0 (-0.2 to 0.2)	.72
Weaning duration, h	18.7 (3.0 to 46.5)	22.0 (3.0 to 44.3)	-0.9 (-4.3 to 1.3)	.36
Spontaneous breathing trials, d	1 (1 to 2)	1 (1 to 2)	0 (0 to 0)	.42
Tracheotomy, median (range), d	0 (0 to 21)	0 (0 to 9)	0 (0 to 0)	.67
Endotracheal intubation, No. (%)	187 (100)	192 (99.5)	0.05 (-0.05 to 1.5)	.99
Use of noninvasive ventilation after extubation, No. (%)	62 (33.1)	72 (37.3)	-4.2 (-13.8 to 5.5)	.39
Successful weaning, No. (%) ^c	118 (74.7)	127 (78.4)	-3.7 (-13.1 to 5.6)	.43

Table 1. Characteristics of the Patients at Baseline

Characteristic	Study Group, Mean (SD)	
	Acetazolamide (n = 187)	Placebo (n = 193)
Age, y	69 (10)	69 (11)
Men, No. (%)	131 (70)	141 (73.1)
SAPS II score ^a	49.4 (13.9)	50 (15.1)
SOFA score ^b	7.2 (3.1)	7.1 (3.2)
BMI	27.2 (8.0)	26.7 (9.1)

Figure 2. Kaplan-Meier Curves for the Cumulative Probabilities of Being Weaned Off Invasive Ventilation



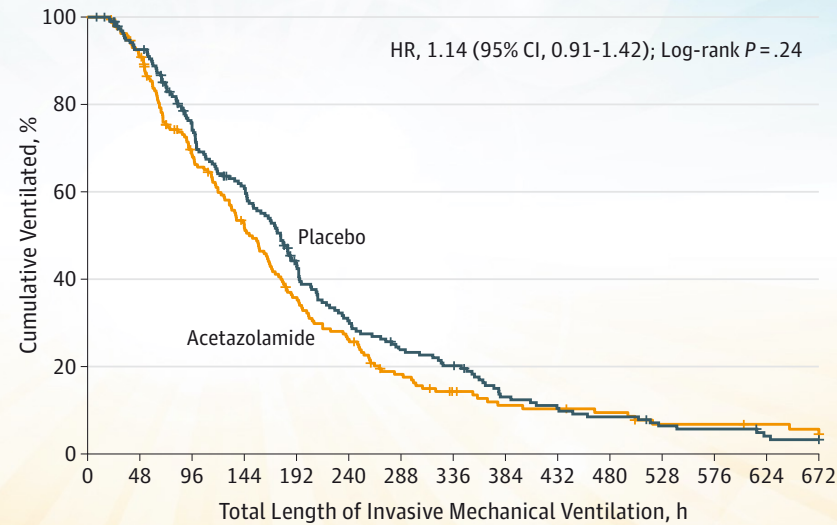


du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

Ventilation mécanique

Figure 2. Kaplan-Meier Curves for the Cumulative Probabilities of Being Weaned Off Invasive Ventilation



No. at risk

	0	48	96	144	192	240	288	336	384	432	480	528	576	624	672
Acetazolamide	187	168	119	89	60	44	28	19	14	13	11	7	7	6	5
Placebo	193	174	137	108	73	51	39	33	20	16	13	9	8	5	4

Table 1. Characteristics of the Patients at Baseline

Characteristic	Study Group, Mean (SD)	
	Acetazolamide (n = 187)	Placebo (n = 193)
Age, y	69 (10)	69 (11)
Men, No. (%)	131 (70)	141 (73.1)
SAPS II score ^a	49.4 (13.9)	50 (15.1)
SOFA score ^b	7.2 (3.1)	7.1 (3.2)
BMI	27.2 (8.0)	26.7 (9.1)

Table 2. Clinical Outcomes and Serious Adverse Events^a

Variable	Group, Median (Interquartile Range)		Between-Group Difference (95% CI)	P Value
	Acetazolamide (n = 187)	Placebo (n = 193)		
Primary Outcome				
Duration of invasive ventilation, h	136.5 (68.7 to 234.7)	163 (86.2 to 242.9)	-16.0 (-36.5 to 4.0)	.17
Secondary Outcomes^b				
Daily				
Serum bicarbonate change, mEq/L	-0.3 (-1.0 to 0.4)	0.3 (-0.2 to 1.3)	-0.8 (-1.2 to -0.5)	<.001
PapO ₂ change, mm Hg	-0.5 (-2.0 to 0.8)	-0.2 (-1.4 to 1)	-0.3 (-0.8 to 0.2)	.25
pH change	0 (-0.01 to 0.02)	0.01 (0 to 0.02)	-0.01 (-0.01 to -0.0)	.008
PapO ₂ /Fio ₂ ratio change, mm Hg	7.8 (-1.5 to 20.3)	3.5 (-5.2 to 13.9)	4.6 (0.6 to 8.6)	.009
Respiratory rate change, cycles/min	0.1 (-0.8 to 1.0)	0.3 (-0.2 to 1.0)	-0.2 (-0.2 to 0.0)	.10
Tidal volume change, mL	4.1 (-7.1 to 28.0)	3.8 (-8.6 to 19.4)	1.3 (-4.2 to 7.5)	.72
Volume-minute change, L/min	0.2 (-0.2 to 0.8)	0.2 (-0.1 to -0.6)	0.0 (-0.2 to 0.2)	.72
Weaning duration, h	18.7 (3.0 to 46.5)	22.0 (3.0 to 44.3)	-9.9 (-4.3 to 1.3)	.36
Spontaneous breathing trials, d				
Success, n (%)	1 (1 to 2)	1 (1 to 2)	0 (0 to 0)	.42
Tracheostomy, median (range), d	0 (0 to 23)	0 (0 to 9)	0 (0 to 0)	.67
Endotracheal intubation, No. (%)	187 (100)	192 (99.5)	0.05 (-0.05 to 1.5)	.99
Use of noninvasive ventilation after extubation, No. (%)	62 (33.3)	72 (37.3)	-4.2 (-13.8 to 5.5)	.39
Successful weaning, No. (%) ^c	118 (74.7)	127 (78.4)	-3.7 (-13.1 to 5.6)	.43

Sevrage VM

TABLE 1. BASELINE CHARACTERISTICS

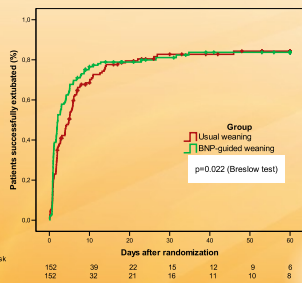
	Usual Care Group (n = 152)	BNP-guided Group (n = 152)
Age, yr	65 (52–74)	66 (55–76)
Sex, male	102 (67.1%)	93 (61.2%)
McCabe class		
0	96 (63.2%)	93 (61.2%)
1	48 (31.6%)	42 (27.6%)
2	8 (5.3%)	17 (11.2%)
SAPS II at ICU admission	44 (34–56)	43 (34–54)
SOFA score at ICU admission	7 (4–9)	7 (4–9)
Duration of invasive mechanical ventilation before inclusion, d		
Median (IQR)	4.4 (2.7–7.8)	5.0 (3.0–9.1)
Mean (SD)	6.5 (5.7)	7.5 (7.6)
Diuretic treatment on the day before randomization	64 (42.1%)	64 (42.1%)

TABLE 2. FLUID MANAGEMENT DURING WEANING

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
patients with at least one daily BNP value > 200 pg/ml during weaning, n (%)	105 (69.1%)	100 (65.8%)	0.541
patients treated at least once with furosemide during weaning, n (%)	108 (71.1%)	124 (81.6%)	<0.001
patients treated at least once with acetazolamide during weaning, n (%)	33 (21.7%)	65 (42.8%)	<0.0001
patients treated at least once with any diuretic during weaning, n (%)	110 (72.4%)	127 (83.6%)	0.019
unplanned furosemide dose during weaning, mg			0.003
Median (IQR)	70 (0–160)	118 (23–229)	
Mean (SD)	180 (244)	180 (231)	
average daily furosemide dose during weaning, mg			<0.0001
Median (IQR)	14 (0 to 40)	40 (9 to 76)	
Mean (SD)	30 (50)	47 (41)	

TABLE 3. MAIN OUTCOMES

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Time to first extubation, h			
Median (IQR)	47.7 (22.9–124.4)	39.8 (26.0–72.4)	0.019
Mean (SD)	92.8 (139.2)	70.6 (96.8)	
Time to successful extubation, h			0.004
Median (IQR)	38.8 (21.3–119.8)	40.4 (28.0–107.0)	
Mean (SD)	112.2 (147.1)	84.2 (127.9)	
Time to successful weaning from intubation and noninvasive ventilation, h			0.051
Median (IQR)	74.4 (17.7–146.5)	49.3 (21.9–146.4)	
Mean (SD)	114.3 (138.4)	107.1 (154.0)	
Ventilator-free days from randomization to Day 14, d			0.006
Median (IQR)	9.7 (2.3–12.9)	12.0 (6.5–13.1)	
Mean (SD)	8.2 (3.2)	9.3 (4.9)	





du 23 au 25
Septembre 2021
PALAIS
DES CONGRÈS
DE PARIS

Sevrage VM

TABLE 1. BASELINE CHARACTERISTICS

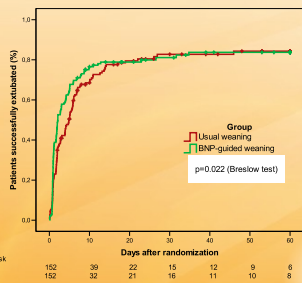
	Usual Care Group (n = 152)	BNP-guided Group (n = 152)
Age, yr	65 (52-74)	66 (55-76)
Sex, male	102 (67.1%)	93 (61.2%)
McCabe class		
0	96 (63.2%)	93 (61.2%)
1	48 (31.6%)	42 (27.6%)
2	8 (5.3%)	17 (11.2%)
SAPS II at ICU admission	44 (34-56)	43 (34-56)
SOFA score at ICU admission	7 (4-9)	7 (4-9)
Duration of invasive mechanical ventilation before inclusion, d		
Median (IQR)	4.4 (2.7-7.8)	5.0 (3.0-9.1)
Mean (SD)	6.5 (5.7)	7.5 (7.6)
Diuretic treatment on the day before randomization	64 (42.1%)	64 (42.1%)

TABLE 2. FLUID MANAGEMENT DURING WEANING

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Patients with at least one daily BNP value \geq 200 pg/ml during weaning, n (%)	105 (69.1%)	100 (65.8%)	0.541
Patients treated at least once with furosemide during weaning, n (%)	108 (71.1%)	124 (81.6%)	0.031
Patients treated at least once with acetazolamide during weaning, n (%)	33 (21.7%)	65 (42.8%)	<0.0001
Patients treated at least once with any diuretic during weaning, n (%)	110 (72.4%)	127 (83.6%)	0.019
Cumulative furosemide dose during weaning, mg			0.003
Median (IQR)	70 (0-160)	118 (23-229)	
Mean (SD)	180 (544)	180 (231)	
Average daily furosemide dose during weaning, mg			<0.0001
Median (IQR)	14 (0 to 40)	40 (9 to 78)	
Mean (SD)	30 (50)	47 (41)	

TABLE 3. MAIN OUTCOMES

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Time to first extubation, h	47.7 (23-124.4)	39.8 (20.0-72.4)	0.019
Median (IQR)	52.8 (19.2)	70.4 (36.6)	
Mean (SD)	68.2 (21.5-119.8)	64.4 (28.0-107.3)	
Time to successful extubation, h	112.2 (47.7)	86.2 (22.9)	0.034
Median (IQR)	124.4 (17.1-165.5)	107.1 (59.0)	
Mean (SD)	134.5 (108.4)	122.0 (85.5-131.1)	
Mean (SD)	9.7 (2.3-12.9)	8.2 (3.2)	0.036





du 23 au 25
Septembre 2021
PALAIS
DES CONGRÈS
DE PARIS

Sevrage VM

TABLE 1. BASELINE CHARACTERISTICS

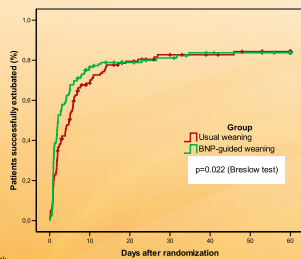
	Usual Care Group (n = 152)	BNP-guided Group (n = 152)
Age, yr	65 (52-74)	66 (55-76)
Sex, male	102 (67.1%)	93 (61.2%)
McCabe class		
0	96 (63.2%)	93 (61.2%)
1	48 (31.6%)	42 (27.6%)
2	8 (5.3%)	17 (11.2%)
SAPS II at ICU admission	44 (34-56)	43 (34-56)
SOFA score at ICU admission	7 (4-9)	7 (4-9)
Duration of invasive mechanical ventilation before inclusion, d		
Median (IQR)	4.4 (2.7-7.8)	5.0 (3.0-9.1)
Mean (SD)	6.5 (5.7)	7.5 (7.6)
Diuretic treatment on the day before randomization	64 (42.1%)	64 (42.1%)

TABLE 3. MAIN OUTCOMES

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Time to first extubation, h			
Median (IQR)	47.7 (22.9-124.8)	39.8 (20.0-72.4)	0.019
Mean (SD)	92.8 (110.2)	70.6 (106.8)	
Time to successful extubation, h			
Median (IQR)	58.6 (23.3-139.8)	42.4 (20.8-107.5)	0.034
Mean (SD)	112.2 (147.1)	86.2 (127.9)	
Time to successful weaning from invasive and noninvasive ventilation, h			
Median (IQR)	74.4 (31.7-160.5)	49.3 (21.9-140.6)	0.051
Mean (SD)	134.3 (187.6)	107.1 (141.0)	
Ventilator-free days from randomization to Day 14, d			
Median (IQR)	9.7 (2.3-12.9)	12.0 (6.5-13.1)	0.026
Mean (SD)	8.2 (5.2)	9.3 (4.9)	

TABLE 2. FLUID MANAGEMENT DURING WEANING

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Patients with at least one daily BNP value > 200 pg/ml during weaning, n (%)	155 (98.1%)	150 (95.8%)	0.541
Patients treated at least once with furosemide during weaning, n (%)	148 (97.1%)	124 (81.6%)	0.031
Patients treated at least once with acetazolamide during weaning, n (%)	33 (22.3%)	43 (28.3%)	<0.0001
Patients treated at least once with any diuretic during weaning, n (%)	110 (72.4%)	127 (83.6%)	0.019
Cumulative furosemide dose during weaning, mg			0.003
Median (IQR)	30 (0-180)	118 (23-239)	
Mean (SD)	180 (440)	180 (241)	
Average daily furosemide dose during weaning, mg			<0.0001
Median (IQR)	14 (0 to 40)	40 (0 to 78)	
Mean (SD)	30 (50)	47 (41)	



Number at risk	0	10	20	30	40	50	60
Usual care	152	39	22	15	12	9	8
BNP-guided	152	32	21	16	11	10	8

Sevrage VM

TABLE 1. BASELINE CHARACTERISTICS

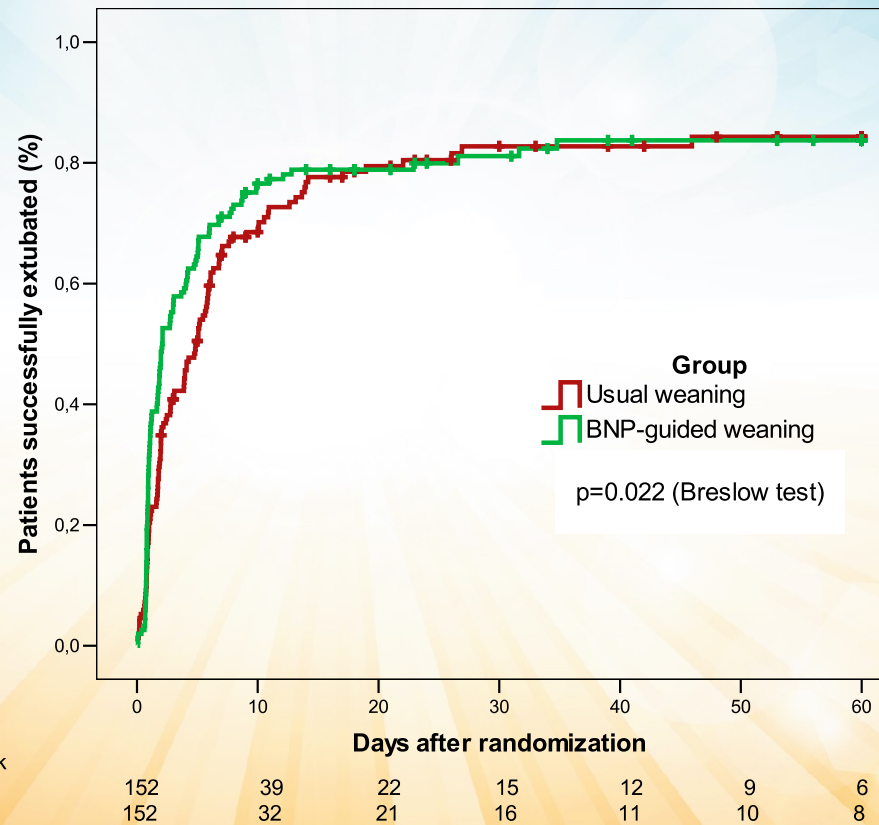
	Usual Care Group (n = 152)	BNP-guided Group (n = 152)
Age, yr	65 (52-74)	66 (55-76)
Sex, male	102 (67.1%)	93 (61.2%)
McCabe class		
0	91 (63.2%)	93 (61.2%)
1	48 (31.6%)	42 (27.6%)
2	8 (5.3%)	17 (11.2%)
SAPS II at ICU admission	44 (34-56)	43 (34-54)
SOFA score at ICU admission	7 (4-9)	7 (4-9)
Duration of invasive mechanical ventilation before inclusion, d	4.4 (2.7-7.8)	5.0 (3.0-9.1)
Median (IQR)		
Mean (SD)	6.5 (5.7)	7.5 (7.6)
Diuretic treatment on the day before randomization	64 (42.1%)	64 (42.1%)

TABLE 2. FLUID MANAGEMENT DURING WEANING

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Patients with at least one daily BNP value > 200 pg/mL during weaning, n (%)	155 (98.1%)	160 (95.8%)	0.341
Patients treated at least once with furosemide during weaning, n (%)	128 (71.1%)	124 (81.6%)	0.031
Patients treated at least once with acetazolamide during weaning, n (%)	31 (22.7%)	45 (44.8%)	<0.0001
Patients treated at least once with any diuretic during weaning, n (%)	110 (72.4%)	127 (83.6%)	0.019
Cumulative furosemide dose during weaning, mg			0.003
Median (IQR)	30 (0-140)	118 (23-239)	
Mean (SD)	180 (146)	160 (211)	
Average daily furosemide dose during weaning, mg			<0.0001
Median (IQR)	14 (0 to 40)	40 (0 to 76)	
Mean (SD)	30 (50)	47 (41)	

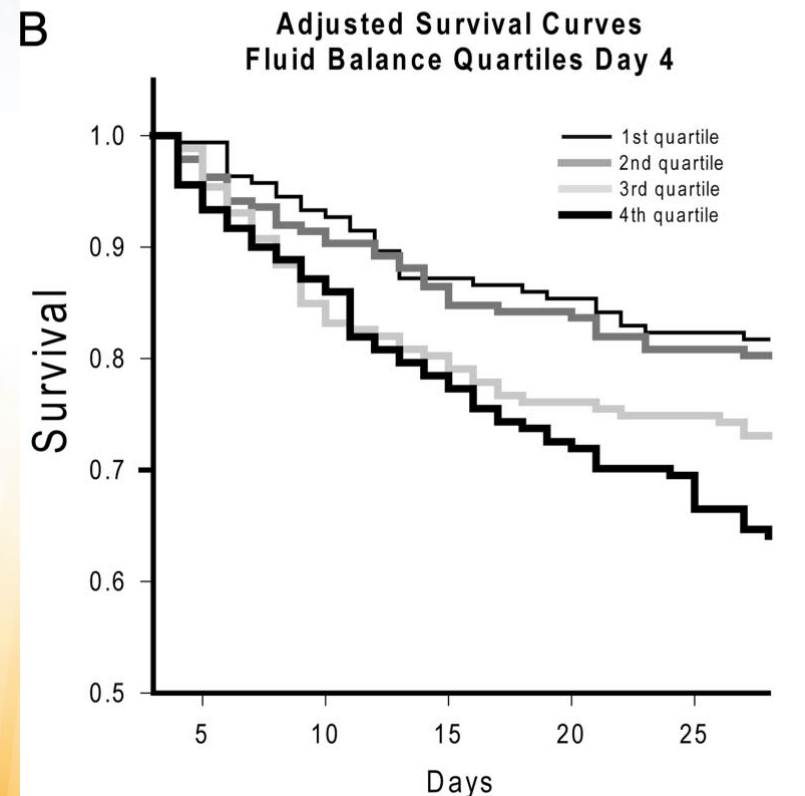
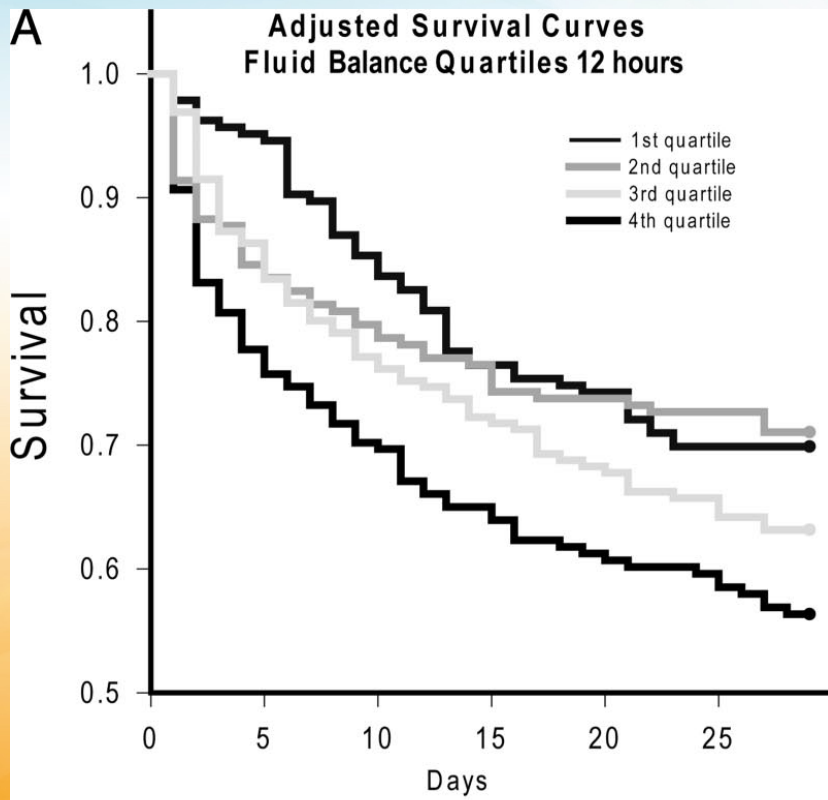
TABLE 3. MAIN OUTCOMES

	Usual Care Group (n = 152)	BNP-guided Group (n = 152)	P Value
Time to first extubation, h			0.019
Median (IQR)	47.7 (22.0-124.8)	39.8 (20.0-72.4)	
Mean (SD)	92.8 (115.2)	75.6 (116.8)	
Time to successful extubation, h			0.034
Median (IQR)	58.6 (23.3-139.8)	42.4 (20.8-107.5)	
Mean (SD)	112.2 (147.1)	86.2 (127.9)	
Time to successful weaning from invasive and noninvasive ventilation, h			0.051
Median (IQR)	74.4 (31.7-140.5)	49.3 (21.9-140.6)	
Mean (SD)	124.5 (157.6)	107.1 (141.0)	
Ventilation-free days from randomization to Day 14, d			0.026
Median (IQR)	9.7 (3.3-13.9)	12.0 (6.5-13.1)	
Mean (SD)	8.2 (5.2)	9.3 (4.9)	



Surcharge et pronostic

Sepsis



Surcharge et pronostic

Brûlé

TABLE 3. Baseline Patient and Injury Characteristics

Variable	Average (range) or %
Total patients	72
Age (yr)	40.6 (18–86)
Weight (kg)	80.6 (49–124)
Total body surface area (TBSA) burn	44.5 (20–90)
Total full-thickness burn	30.7 (1–90)
Inhalation injury	42%
Time to admission postinjury (hr)	3.4 (0–12)
Admitted on ventilator	57%
Apache II score	20.1 (6–36)
Initial base deficit	4.5 (–9 to 15)
Burn mechanism (%)	
Flame	76
Flash	11
Other	13
Gender (male) (%)	71

TABLE 7. Effect of Proportion of Fluid Above Volume Predicted

Outcome	OR (95% CI)*
<u>ARDS</u>	
0%–25% above predicted	0.52 (0.17–7.3)
>25% above predicted	1.69 (0.48–5.9)
<u>Pneumonia</u>	
0%–25% above predicted	0.71 (0.23–2.1)
>25% above predicted	5.67 (1.1–29.9)
<u>Multiple organ failure</u>	
0%–25% above predicted	0.94 (0.24–3.7)
>25% above predicted	1.6 (0.38–6.6)
<u>Bloodstream infections</u>	
0%–25% above predicted	1.12 (0.17–7.33)
>25% above predicted	2.91 (0.51–16.5)
<u>Death</u>	
0%–25% above predicted	0.42 (0.08–2.5)
>25% above predicted	5.33 (1.4–20.4)

*Reference: less than or equal to predicted volume.

Surcharge et pronostic

Pédiatrie

Table 3 Primary disease

Primary disease	Total 113 patients	
	Number	% of total patients
Heart disease	41	36.3
Primary renal disease	6	5.3
Bone marrow transplant	12	10.6
Oncologic disease	10	8.9
Metabolic	8	7.1
Poisoning	2	1.8
Liver disease	15	13.3
Sepsis without underlying disease	8	7.1
Congenital diaphragmatic hernia	5	4.4
Other	6	5.3

Table 6 Results of logistic regression analysis assessing odds of death based on degree of fluid overload at CRRT initiation

Variable ^a	Odds ratio	95% CI	p-Value
Univariate analysis			
Method 1 fluid overload	1.056	1.025, 1.087	0.0002
Method 2 fluid overload	1.044	1.019, 1.069	0.0005
Method 3 fluid overload	1.045	1.022, 1.07	0.0002
Multivariate analysis^b			
Method 1 fluid overload	1.04	1.00, 1.07	0.0529
Method 2 fluid overload	1.03	0.99, 1.07	0.0829
Method 3 fluid overload	1.03	0.99, 1.06	0.1

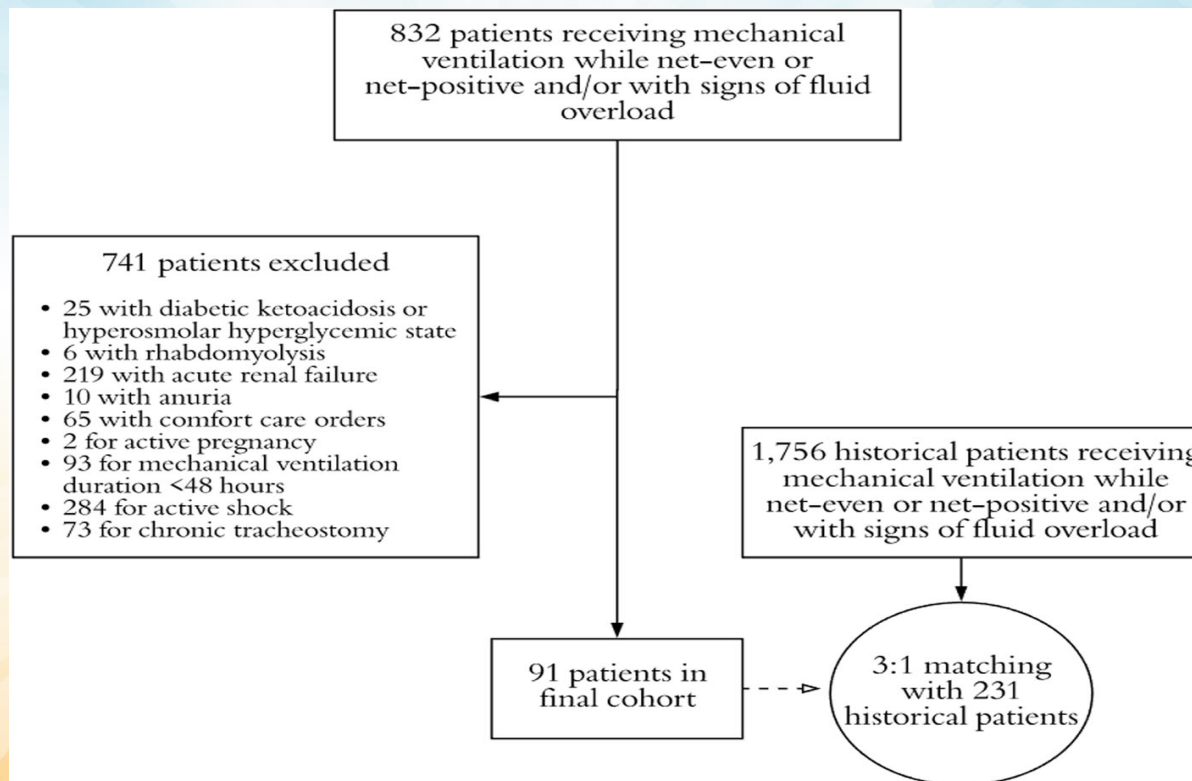
Diurétiques et pronostic?

Table 2 Pharmacotherapy

Parameter	Historical cohort (n=273)	Intervention cohort (n=91)	p value
Furosemide dosing			
Starting dose (mg) ^a	40 (20-40)	40 (40-40)	0.003
Day one total daily dose (mg) ^b	40 (40-40)	80 (40-120)	< 0.0001
Day two total daily dose (mg) ^b	0 (0-40)	80 (20-120)	< 0.0001
Day three total daily dose (mg) ^b	0 (0-20)	0 (0-40)	0.0007
Total cumulative dose (mg) ^b	80 (40-200)	240 (120-420)	< 0.0001

Table 3 Clinical outcomes

Parameter	Historical cohort (n=273)	Intervention cohort (n=91)	p value
Clinical outcomes			
72 h fluid balance (mL) ^a	265 (-2283-3025)	-2257 (-5676-928)	< 0.00
48 h fluid balance (mL) ^a	309 (-1267-2434)	-1796 (-3884-1092)	< 0.00
24 h fluid balance (mL) ^a	101 (-903-1622)	-692 (-1893-497)	0.0002
Ventilator free days (days) ^a	19 (10-23)	20 (15-23)	0.098
Overall adverse event ^b	74 (27.1)	37 (40.6)	0.015
Ventilator days (days) ^a	8 (5-13)	5 (5-12)	0.441
Furosemide to extubation (hours) ^a	70 (24-147)	58 (23-122)	0.282
Re-intubation rate ^c	57 (20.8)	17 (18.6)	0.652
ICU free days (days) ^a	17 (7-23)	19 (13-22)	0.830
ICU days (days) ^a	86 (62-113)	81 (59-124)	0.513
In-hospital mortality ^d	44 (16.1)	5 (5.5)	0.008
Safety outcomes			
Bolus administration after furosemide ^e	4 (1.5)	0 (0)	0.576
Vasopressor administration after furosemide ^e	65 (23.8)	19 (20.9)	0.566
Tachyarrhythmia ^f	50 (18.3)	15 (16.4)	0.693
In-hospital mortality ^d	44 (16.1)	5 (5.5)	0.008
RRT receipt in ICU ^g	17 (6.2)	0 (0)	< 0.00
RRT dependence at discharge ^g	14 (5.1)	0 (0)	0.025
Acute kidney injury ^h	62 (22.7)	22 (24.2)	0.775
Hypokalemia ⁱ	0	3 (3.3)	0.015
Hypertension ^j	19 (6.9)	19 (20.9)	0.001
Metabolic alkalosis ^k	3 (1.1)	1 (1.1)	1.000



Diurétiques et pronostic?

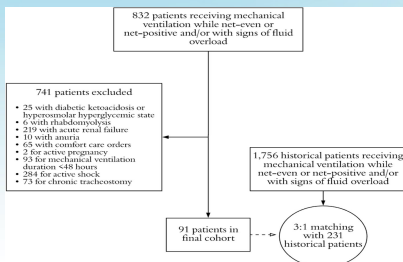


Table 3 Clinical outcomes

Parameter	Historical cohort (n = 273)	Intervention cohort (n = 91)	p value
72 h fluid balance (mL) ^a	265 (-2283-3025)	-2257 (-5676-928)	< 0.001
48 h fluid balance (mL) ^a	309 (-1267-2434)	-1799(-3884-1082)	< 0.001
24 h fluid balance (mL) ^a	101 (-963-1622)	-661(-1833-497)	0.002
Ventilator-free days (days) ^a	19 (10-23)	20 (11-23)	0.098
Overall adverse event ^a	74 (27.1)	37 (40.6)	0.015
Ventilator days (days) ^a	8 (5-13)	5 (5-12)	0.441
Furosemide to entubation (hours) ^a	70 (24-147)	58 (23-122)	0.282
Re-intubation rate ^a	57 (20.8)	17 (18.6)	0.652
ICU-free days (days) ^a	17 (7-23)	19 (13-22)	0.830
ICU days (days) ^a	86 (62-113)	81 (59-124)	0.513
In-hospital mortality ^a	44 (16.1)	5 (5.5)	0.008

Safety outcomes

Bolus administration after furosemide ^a	4 (1.5)	0 (0)	0.576
Vasopressor administration after furosemide ^a	65 (23.8)	19 (20.9)	0.566
Tachyarrhythmia ^a	50 (18.3)	15 (16.4)	0.693
In-hospital mortality ^a	44 (16.1)	5 (5.5)	0.008
RRT receipt in ICU ^a	17 (6.2)	0 (0)	< 0.001
RRT dependence at discharge ^a	14 (5.1)	0 (0)	0.025
Acute kidney injury ^a	62 (22.7)	22 (24.2)	0.775
Hypokalemia ^a	0	3 (3.3)	0.015
Hypertatemia ^a	19 (6.9)	19 (20.9)	0.001
Metabolic alkalosis ^a	3 (1.1)	1 (1.1)	1.000

Table 2 Pharmacotherapy

Parameter	Historical cohort (n = 273)	Intervention cohort (n = 91)	p value
Furosemide dosing			
Starting dose (mg) ^a	40 (20-40)	40 (40-40)	0.003
Day one total daily dose (mg) ^a	40 (40-60)	80 (40-120)	< 0.0001
Day two total daily dose (mg) ^a	0 (0-40)	80 (20-120)	< 0.0001
Day three total daily dose (mg) ^a	0 (0-20)	0 (0-80)	0.0007
Total cumulative dose (mg) ^a	80 (40-200)	240 (120-420)	< 0.0001

Diurétiques et pronostic?

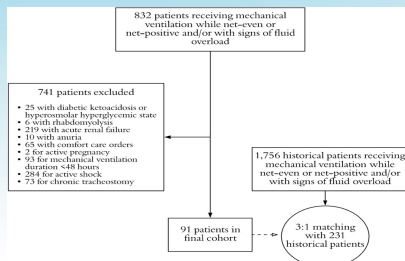


Table 2 Pharmacotherapy

Parameter	Historical cohort (n=273)	Intervention cohort (n=91)	p value
Furosemide doses			
Sating dose (mg) ^a	40 (20-40)	40 (40-40)	0.003
Day one total daily dose (mg) ^a	40 (40-40)	80 (40-120)	<0.0001
Day two total daily dose (mg) ^a	0 (0-40)	80 (20-120)	<0.0001
Day three total daily dose (mg) ^a	0 (0-20)	0 (0-40)	0.0007
Total cumulative dose (mg) ^a	80 (40-200)	240 (120-420)	<0.0001

Safety outcomes	Historical cohort (n=273)	Intervention cohort (n=91)	p value
Bolus administration after furosemide ^a	4 (1.5)	0 (0)	0.576
Vasopressor administration after furosemide ^b	65 (23.8)	19 (20.9)	0.566
Tachyarrhythmia ^b	50 (18.3)	15 (16.4)	0.693
In-hospital mortality ^c	44 (16.1)	5 (5.5)	0.008
RRT receipt in ICU ^d	17 (6.2)	0 (0)	< 0.001
RRT dependence at discharge ^d	14 (5.1)	0 (0)	0.025
Acute kidney injury ^e	62 (22.7)	22 (24.2)	0.775
Hypokalemia ^f	0	3 (3.3)	0.015
Hypenatremia ^g	19 (6.9)	19 (20.9)	0.001
Metabolic alkalosis ^h	3 (1.1)	1 (1.1)	1.000

Table 3 Clinical outcomes

Parameter	Historical cohort (n = 273)	Intervention cohort (n = 91)	p value
Clinical outcomes			
72 h fluid balance (mL) ^d	265 (- 2283-3025)	- 2257 (- 5676-920)	< 0.001
48-h fluid balance (mL) ^d	309 (- 1267-2434)	- 1799(- 3884-1092)	< 0.001
24-h fluid balance (mL) ^a	101 (- 963-1622)	- 692 (- 1833-697)	0.0002
Ventilator-free days (days) ^a	19 (10-22)	20 (15-23)	0.098
Overall adverse event ^{b,e}	74 (27.1)	37 (40.6)	0.015
Ventilator days (days) ^a	8 (5-13)	5 (5-12)	0.441
Furosemide to extubation (hours) ^a	70 (24-147)	58 (23-122)	0.282
Re-intubation rate ^b	57 (20.8)	17 (18.6)	0.652
ICU-free days (days) ^a	17 (7-21)	19 (13-22)	0.030
ICU days (days) ^a	8.6 (6.2-13.5)	8.1 (5.9-12.8)	0.513
In-hospital mortality ^c	44 (16.1)	5 (5.5)	0.008

Diurétiques et pronostic?

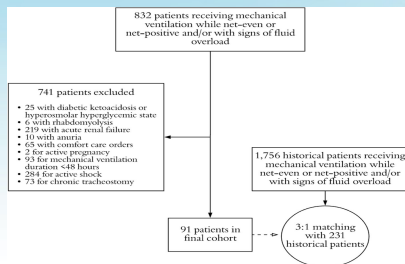


Table 2 Pharmacotherapy

Parameter	Historical cohort (n=273)	Intervention cohort (n=91)	p value
Furosemide doses			
Starting dose (mg) ^a	40 (20-40)	40 (40-40)	0.003
Day one total daily dose (mg) ^a	40 (40-40)	80 (40-120)	<0.001
Day two total daily dose (mg) ^a	0 (0-40)	80 (20-120)	<0.001
Day three total daily dose (mg) ^a	0 (0-20)	0 (0-40)	0.007
Total cumulative dose (mg) ^a	80 (40-200)	240 (120-420)	<0.001

Table 3 Clinical outcomes

Parameter	Historical cohort (n=273)	Intervention cohort (n=91)	p value
Clinical outcomes			
72 h fluid balance (mL) ^d	265 (-2283-3025)	-2257 (-5676-920)	<0.001
48 h fluid balance (mL) ^d	309 (-1267-2434)	-1799(-3884-1052)	<0.001
24 h fluid balance (mL) ^d	101 (-963-1622)	-692 (-1833-697)	0.0002
Ventilator-free days (days) ^e	19 (10-22)	20 (15-23)	0.098
Overall adverse event ^g	74 (27.1)	37 (40.6)	0.015
Ventilator days (days) ^e	8 (5-13)	5 (5-12)	0.441
Furosemide to extubation (hours) ^a	70 (24-147)	58 (23-122)	0.282
Re-intubation rate ^b	57 (20.8)	17 (18.6)	0.652
ICU-free days (days) ^a	17 (7-21)	19 (13-22)	0.030
ICU days (days) ^a	8.6 (6.2-13.5)	8.1 (5.9-12.8)	0.513
In-hospital mortality ^c	44 (16.1)	5 (5.5)	0.008

Safety outcomes

Bolus administration after furosemide ^c	4 (1.5)	0 (0)	0.576
Vasopressor administration after furosemide ^b	65 (23.8)	19 (20.9)	0.566
Tachyarrhythmia ^b	50 (18.3)	15 (16.4)	0.693
In-hospital mortality ^c	44 (16.1)	5 (5.5)	0.008
RRT receipt in ICU ^c	17 (6.2)	0 (0)	<0.001
RRT dependence at discharge ^c	14 (5.1)	0 (0)	0.025
Acute kidney injury ^f	62 (22.7)	22 (24.2)	0.775
Hypokalemia ^c	0	3 (3.3)	0.015
Hypernatremia ^b	19 (6.9)	19 (20.9)	0.001
Metabolic alkalosis ^c	3 (1.1)	1 (1.1)	1.000



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

IRIHS-REA

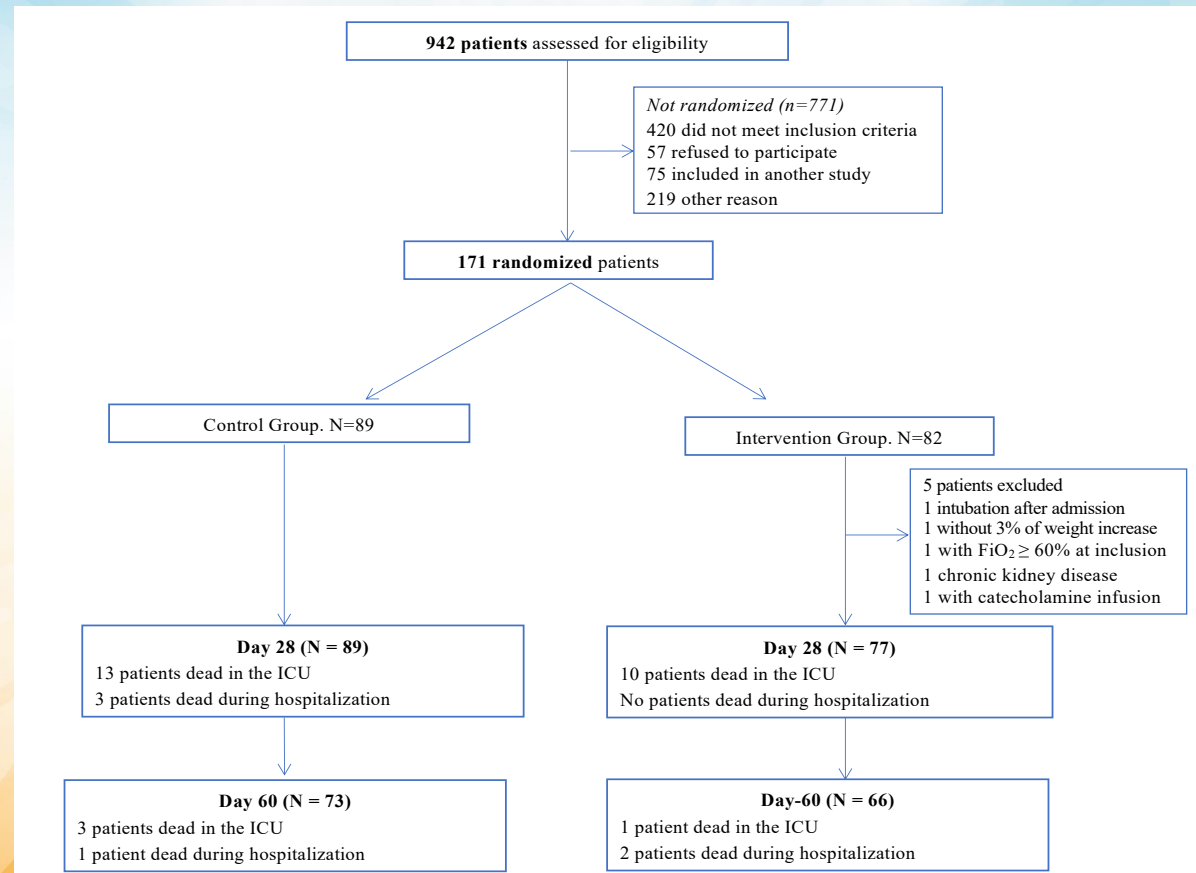
Design

- Etude multicentrique
- Randomisée-contrôlée
- Simple aveugle
- Critère ppal: diminuer l'inflation hydro-sodée
- Critères secondaires: tolérance (rein, cœur, métabolique) / efficacité

Protocole

- Ventilation mécanique invasive ≥ 24 heures
- Sevrage NAD
- Inflation poids: Augmentation $\geq 3\%$ par rapport au « poids sec »
- Intervention: Furosemide ou autre diurétique QSP poids sec jusqu'au sevrage de la VM
- Contrôle

Flowchart



Démographie

	Groupe Contrôle N=89	Groupe Diurétiques N=77
Age	66 [60 - 74]	66 [58 - 72]
Genre F/H	28(31.5%) / 61(68.6%)	16(20.8%) / 61(79.2%)
SAPS II	53 [45 - 59]	52 [41 - 58]
SOFA	7 [5 - 10]	8 [6 - 10]
IMC	25.5 [22.6 - 29.2]	28.4 [25.5 - 34.5]
HTA	13 (14.6%)	5 (6.5%)
BPCO	10 (11.2%)	5 (6.5%)
IRC	3 (3.4%)	1 (1.3%)
Diurétiques au long cours	11 (12.4%)	8 (10.4%)
Diabète	9 (10.1%)	11 (14.3%)
Admission		
Sepsis/choc septique	28 (31.4%)	21 (27.2%)
Détresse respi	42 (47.2%)	33 (42.9%)
Trauma	7 (7.9%)	6 (7.8%)
EER/AKI avant inclusion	27 (30.3%)	21 (27.3%)

Inflation hydro-sodée

	Contrôle N=89	Intervention N=77	Difference 95% IC	P
Analyse première				
Cas complets (N=144)	6.4 [5-11.2]	1.4 [1-4.5]		<0.001
Imputation multiple (N=160)			-4.9 [-7.4;-2.5]	<0.001
Analyse de sensibilité				
Biais maximal (N=160)	4.5 [-1.5;10.5]	1.5 [-2;7.7]	-0.5 [-3.2;2.3]	0.7
Per protocol (N=130)	5 [0.5;11.3]	1 [-2.5;4.5]	-4.8 [-7.2;-2.2]	<0.001

Critères secondaires

Efficacité

	Contrôle N=89	Intervention N=77	P
Ventilation mécanique			
Durée (j)	14 [8-22]	12 [8-21]	0.7
Après rando (j)	7 [3-17]	6 [2-14]	0.2
VFD à J-28	19 [3-24]	22 [9-25]	0.3
Échec d'extubation	11 (15.3%)	6 (9%)	0.3
Durée séjour (j)	18 [10-32]	18 [11-29]	0.4
Mortalité en réa	16 (18%)	11 (14%)	0.5
Durée hôpital (j)	36 [22-55]	32 [18-53]	0.6
Mortalité à J-60	20 (22.5%)	13 (16.9%)	0.5

Critères secondaires

Tolérance rénale-métabolique

	Contrôle N=89	Intervention N=82	P
RIFLE (N)			0.2
None	22 (25.3%)	30 (40%)	
Risk	33 (37.9%)	25 (33.3%)	
Natrémie ≤ 135mmol/L (N)	42 (47.2%)	33 (42.9%)	0.7
Natrémie ≥ 145mmol/L (N)	40 (44.9%)	40 (52%)	0.5
Hypokaliémie (N)	51 (57.3%)	53 (68.8%)	0.1
Durée hypokaliémie (j)	1 [0-2]	1 [0-4]	0.2

Critères secondaires

Tolérance cardiaque

	Contrôle N=89	Intervention N=82	P
Cardiac rhythm troubles (N)			
Atrial fibrillation	14 (15.3%)	9 (11.7%)	0.5
Torsade de pointes	0	1 (1.3%)	0.5
Ventricular tachycardia	2 (2.3%)	2 (2.6%)	0.9
Ventricular fibrillation	2 (2.3%)	1 (2.6%)	0.9



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

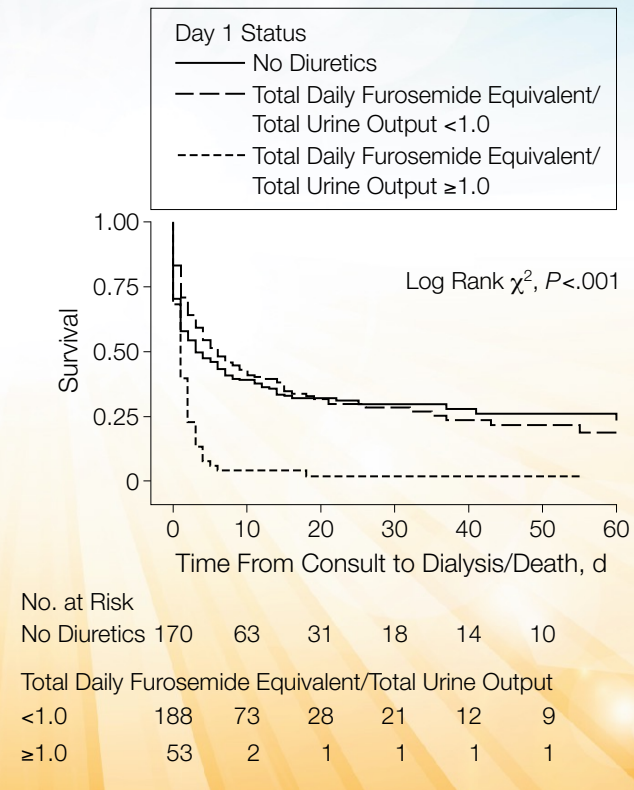
Intérêts des diurétiques

- Lutte efficace contre l'inflation hydro-sodée à la phase sub-aiguë en réanimation
- Intérêt dans le sevrage de la VM
- Données rassurantes sur la tolérance
- Manque de preuve formelles sur l'efficacité des diurétiques

Toxicité rénale!

Diuretics, Mortality, and Nonrecovery of Renal Function in Acute Renal Failure

Figure 2. Time to Death or Dialysis From Day of Consultation in Intensive Care Unit



Toxicité rénale??

Table 1 Baseline characteristics between groups before matching

Variables	Non-diuretic group <i>n</i> = 6269	Furosemide group <i>n</i> = 7885	<i>P</i> value	SMD
AKI stage, <i>n</i> (%)			< 0.001	0.132
Stage 1	1953(31.2)	2293(29.1)		
Stage 2	2715(43.3)	3908(49.6)		
Stage 3	1601(25.5)	1684(21.4)		
Age	67.8 (54.7,78.9)	69.9 (59.2,79.4)	< 0.001	0.167
Gender, male, <i>n</i> (%)	3503 (55.9)	4419 (56.0)	0.844	0.003

	Non-diuretic group <i>n</i> = 6269	Furosemide group <i>n</i> = 7885	<i>P</i> value	OR	95% CI	SMD
Pre-matched cohort						
In-hospital mortality, <i>n</i> (%)	1362(21.7)	1001(12.7)	< 0.001	0.63	0.53	0.69
30-day mortality, <i>n</i> (%)	198(3.1)	167(2.1)	< 0.001	0.66	0.45	0.70
Recovery of renal function, <i>n</i> (%)	2084(33)	4202(53.4)	< 0.001	1.29	1.21	1.38
Length of ICU stay (median [IQR])	23(24, 4.8)	4(1.25, 1.4)	< 0.001	1.44	1.28	1.62
Length of hospital stay (median [IQR])	107(63, 142)	103(68, 143)	0.011	1.07	1.02	1.08
Post-matched cohort						
In-hospital mortality, <i>n</i> (%)	174(2.8)	103(1.3)	< 0.001	0.67	0.50	0.74
30-day mortality, <i>n</i> (%)	14(0.22)	15(0.19)	< 0.001	0.69	0.44	0.75
Recovery of renal function, <i>n</i> (%)	262(4.2)	299(3.8)	< 0.001	1.44	1.31	1.57
Length of ICU stay (median [IQR])	4(1.0, 1.1)	4(1.0, 1.2)	0.201	1.08	0.88	1.02
Length of hospital stay (median [IQR])	108(64, 146)	103(63, 144)	0.002	1.11	1.04	1.05

Toxicité rénale??

	Non-diuretic group	Furosemide group	P value	HR	Lower 95% CI	Upper 95% CI
<u>Pre-matched cohort</u>	<i>n</i> = 6269	<i>n</i> = 7885				
Primary outcome						
In-hospital mortality, <i>n</i> (%) ^a	1363(21.7)	1001(12.7)	< 0.001	0.63	0.58	0.69
Secondary outcomes						
90-day mortality, <i>n</i> (%) ^a	1981(31.6)	1673(21.2)	< 0.001	0.66	0.61	0.70
Recovery of renal function, <i>n</i> (%) ^b	2939(46.9)	4209(53.4)	< 0.001	1.29	1.21	1.38
Length of ICU stay, [median (IQR)] ^c	3.91(2.8, 6.8)	4.13(2.9, 7.4)	0.003	1.44	1.28	1.62
Length of hospital stay, [median (IQR)] ^c	9.57(6.0, 16.2)	10.08(6.8, 16.3)	0.013	1.37	1.12	1.68
<u>Post-matched cohort</u>	<i>n</i> = 4427	<i>n</i> = 4427				
Primary outcome						
In-hospital mortality, <i>n</i> (%) ^a	974(22.0)	635(14.3)	< 0.001	0.67	0.60	0.74
Secondary outcomes						
90-day mortality, <i>n</i> (%) ^a	1442(32.6)	1054(23.8)	< 0.001	0.69	0.64	0.75
Recovery of renal function, <i>n</i> (%) ^b	2620(59.2)	2991(67.6)	< 0.001	1.44	1.31	1.57
Length of ICU stay, [median (IQR)] ^c	4.1(2.9, 7.1)	4.1(2.9, 7.2)	0.221	1.28	0.89	1.62
Length of hospital stay, [median (IQR)] ^c	10.0(6.4, 16.9)	10.5(6.5, 16.4)	0.032	1.71	1.04	2.85

Table 1 Baseline characteristics between groups before matching

Variables	Non-diuretic group <i>n</i> = 6269	Furosemide group <i>n</i> = 7885	P value	SMD
All stages, <i>n</i> (%)			< 0.001	0.112
Stage 1	1953(31.2)	2392(30.3)		
Stage 2	2758(44.0)	3086(39.1)		
Stage 3	1602(25.3)	1887(23.9)		
Age	67.8 (54.7-78.9)	69.0 (52.5-77.4)	< 0.001	0.167
Gender, male, <i>n</i> (%)	3028 (48.3)	4419 (55.9)	0.041	0.003



du 23 au 25
Septembre 2021

PALAIS
DES CONGRÈS
DE PARIS

Conclusion

- Intérêt de la diminution de l'inflation hydro-sodée en réanimation
- Efficacité potentielle dans le sevrage VM
- Données rassurantes sur la tolérance