

Les complications hémodynamiques

Les états de choc cardio-vasculaire

Choc hypovolémique

*Le volume contenu dans le compartiment intravasculaire
n'assure pas une perfusion tissulaire adéquate*

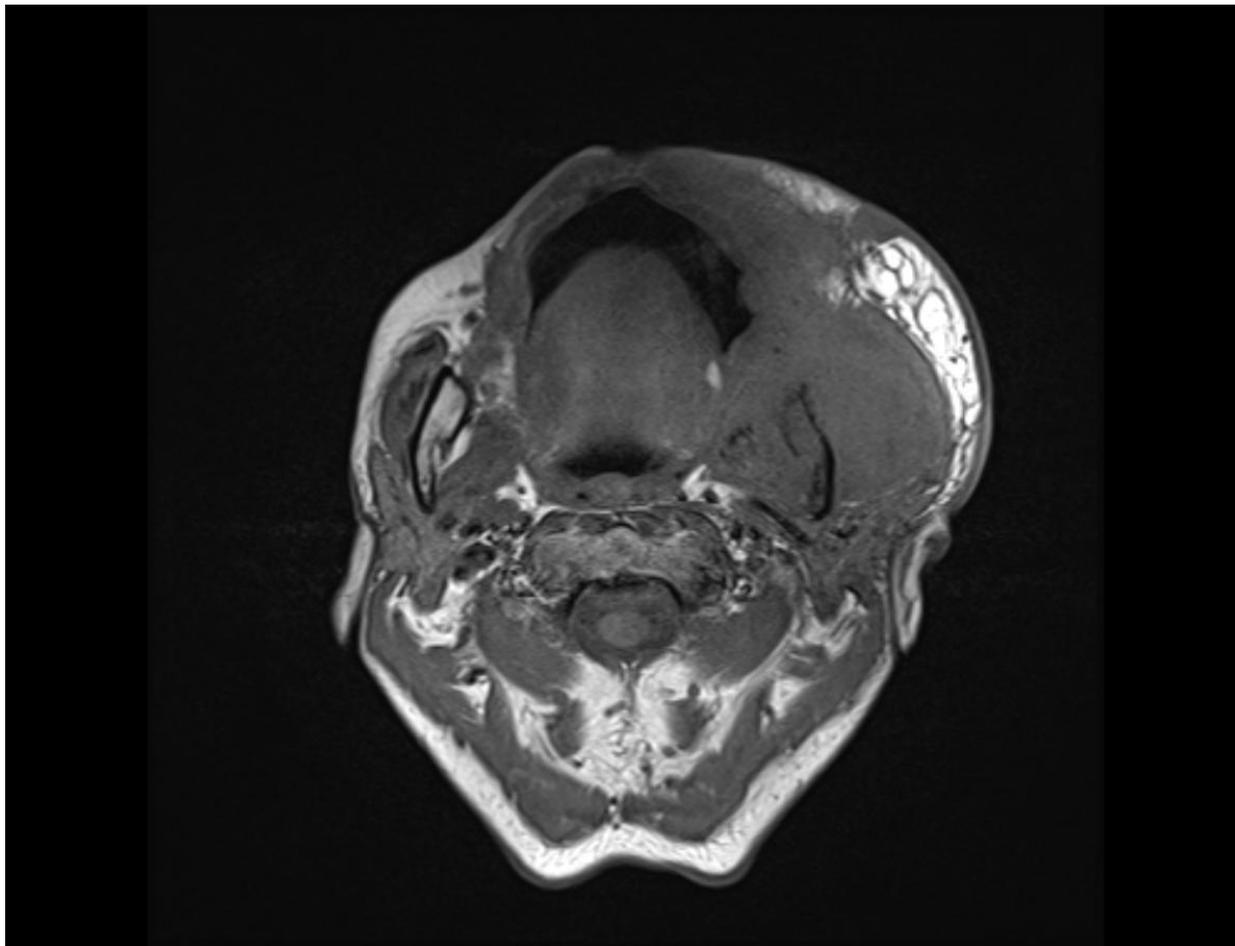
Principales étiologies

A. Par pertes externes de liquide

- pertes de sang : **hémorragies externes**
- pertes de plasma : brûlures, lésions exsudatives
- pertes hydro-électrolytiques:
 - pertes digestives : **vomissements, diarrhées**
 - pertes cutanées : **déshydratation** (fièvre)
 - pertes rénales : *diabète sucré, diabète insipide, diurétiques, crise addisonienne, hypercalcémie*

B. Par séquestration interne du liquide

- **hémorragies internes** : fractures, **digestives** (ulcus, varices œsophagiennes,...), hémothorax, hémopéritoine, hématome rétro-péritonéal, anévrisme disséquant de l'aorte, pancréatite hémorragique, infarctus intestinal ...
- **3e espace** : ascite, obstruction intestinale, épanchement pleural
- **choc anaphylactique**
- *phéochromocytome*



Rupture de l'artère carotide

Tableau clinique

- Complication majeure observée chez les patients atteints d'une tumeur cervico-faciale
- Facteurs favorisants: chirurgie, radiothérapie, infection locale, nécrose tumorale, malnutrition
- Hémorragie externe massive, hématome compressif, détresse respiratoire par compression trachéal

Attitude thérapeutique

- Compression manuelle de l'artère qui saigne
- Transfert en salle d'opération en vue ligature chirurgicale
- Installation d'une voie veineuse etpanseurs
- Oxygénothérapie

Pronostic

- 1/3 décès
- 1/3 séquelles neurologiques (hémiparésie, hémiplégie, psychiques ...)
- 1/3 survie sans séquelle

Phéochromocytome



Accidents tensionnels aigus

Crise d'hypertension paroxystique (>180/100 mm Hg, parfois très élevée)

- spontanée ou déclenchée par un effort, un traumatisme, une palpation, un acte agressif !

Accès hypertensif malin : > 150 (D) / 300 (S) mm Hg !:

- tableau d'encéphalopathie hypertensive (amaurose, coma, convulsions)

Choc adrénergique : avec tachycardie très rapide (>200/min)

- secondaire à un traumatisme (ex. chute, manipulation brutale, anesthésie)
- suivi d'oscillations très rapides (80 → 300 mm Hg !)

Collapsus vasculaire: après l'ablation de la tumeur (immédiat)

Complications myocardiques :

- insuffisance cardiaque
- OPA
- nécrose myocardique

Traitement

- **crise d'hypertension artérielle** : α -bloquant
 - phentolamine
 - labétalol
- **collapsus vasculaire** : expanseurs + corticoïdes
- **choc adrénérgique** : β -bloquants (+hydrocortisone 100 à 200 mg i.v.)
 - propranolol 5 mg i.v. en 5 min, à répéter évt (but = réduire la tachycardie)

Pheochromocytoma Crisis in the ICU: A French Multicenter Cohort Study With Emphasis on Rescue Extracorporeal Membrane Oxygenation

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(Crit Care Med 2017; 45:e657–e665)



Les réactions anaphylactiques

Définition

= réaction aiguë (en quelques secondes à minutes),
systémique, potentiellement mortelle, à un
antigène entraînant la libération de médiateurs
(histamine, sérotonine) par les mastocytes

Diagnostic différentiel

- **Réaction anaphylactique** : médiée par IgE (nécessite exposition préalable à l'Ag)
- **Réaction anaphylactoïde** : effet direct du médicament sur les mastocytes

En cause

Cancers à risque

- LLA: asparaginase
- lymphomes: bléomycine (fièvre)
- tumeurs gynécologiques: taxanes

Anticancéreux: TOUS

Réactions d'hypersensibilité risque de choc anaphylactique

Très fréquent (> 10⁰%):

- paclitaxel
- docétaxel
- asparaginase

Non rare (1-10⁰%):

- cisplatine
- carboplatine
- bléomycine
- étoposide
- Méthotrexate
- Anticorps monoclonaux
- ...

Tableau clinique

- Contexte évocateur (injection médicament,...)
- Antécédents allergiques
- douleurs abdominales, vomissements, diarrhée
- anxiété, agitation

Etat de choc: hypotension, tachycardie

- « chaud »: pas de marbrures, érythème diffus
- signes associés:
 - **bronchospasme**
 - **œdème laryngé** (+ face et paupières)
 - **urticaire**



Pronostic

Décès rapide en l'absence de traitement:

- par complications respiratoires : 70%
- par complications cardiovasculaires : 25%

Traitement

- Arrêt de toute perfusion en cours
- mise en décubitus dorsal, jambes surélevées
- adrénaline (épinéphrine): 0,5 à 1 mg SC (avec rinçure en IVD), à répéter en IVD toutes les 5 min si choc persistant
- remplissage vasculaire
- oxygénothérapie
- corticothérapie: 120 mg méthylprednisolone IVD
- surveillance USI 12h: risque de récurrence!

Prévention

- Systématique en cas de traitement par taxanes: paclitaxel, docétaxel
- corticoïdes, antihistaminiques antiH1 et antiH2 12h, 6h et 30 min avant l'injection du cytotoxique
- sous monitoring si antécédents de réaction grave



*Agence française de sécurité sanitaire
des produits de santé*

**Direction de l'Évaluation
des Médicaments et des Produits Biologiques**
Département de Pharmacovigilance

REPUBLIQUE FRANÇAISE

Saint-Denis, le 24 mars 2009

COMMISSION NATIONALE DE PHARMACOVIGILANCE

Compte rendu de la réunion du mardi 27 janvier 2009

IV - ENQUETE NATIONALE DE PHARMACOVIGILANCE : REACTIONS ANAPHYLACTOÏDES ET ANAPHYLACTIQUES GRAVES SURVENUES PENDANT ET JUSQU'A 24 HEURES APRES LA PERFUSION D'UN SEL DE PLATINE

Le CRPV de Dijon présente les résultats d'une enquête de pharmacovigilance relative aux réactions anaphylactoïdes et anaphylactiques graves survenues pendant et jusqu'à 24 heures après la perfusion d'un sel de platine.

Ces résultats ont fait l'objet d'une présentation au comité technique de pharmacovigilance du 7 octobre 2008.

3. Résultats et discussions :

284 des 410 observations transmises par les laboratoires ont été retenues pour l'analyse. La moitié des cas analysés (144 cas) correspondent à des cas notifiés aux CRPV :

- L'âge moyen des patients est proche pour les trois médicaments et correspond à celui de survenue de tumeurs de l'ovaire et du côlon (principales indications). Bien qu'un certain nombre de facteurs de risque soit décrit dans la littérature (allergie médicamenteuse, atopie, tabagisme lors d'exposition professionnelle, ethnie en Asie), peu d'informations sont retrouvées dans les observations analysées.

- Protocoles de chimiothérapie concernés :

- 38 patients (13%) recevaient le sel de platine en monothérapie ou bien associé à des traitements dont la responsabilité dans la survenue de l'HS était exclue.

- 29 cas (10%) sont survenus au cours d'une première ligne (L1) de traitement

- 67 patients (23%) avaient déjà reçu des sels de platine

- Le cycle de survenue des hypersensibilités aux sels de platine se situe aux alentours du 6^{ème} cycle. Lors de la reprise de traitement par sel de platine, la réaction survient préférentiellement vers le 3^{ème} cycle. Ces données correspondent à celles retrouvées dans la littérature.

- Délai d'apparition au sein du cycle de chimiothérapie : 75% des réactions surviennent pendant la perfusion ou en fin de perfusion.

- Les effets indésirables ont été classés selon les critères de sévérité de Ring et Messmer¹ : dans 15% des cas, seule une atteinte cutanée isolée (grade I) a été rapportée et 30% des cas correspondaient à des symptômes modérés d'hypersensibilité (grade II).

Parmi les patients ayant présenté un facteur de sévérité (grade III et IV), dix sept patients (6%) ont présenté un arrêt cardio-respiratoire.

- Dans la majorité des cas, l'évolution était favorable sous traitement symptomatique. Quatre décès sont rapportés.

- Réadministration :

- *Avec le même sel de platine* : Parmi les 284 dossiers, 78 patients (27%) ont présenté une réadministration positive du même sel de platine. Neuf patients (3%) n'ont pas eu de réaction lors de la réadministration.

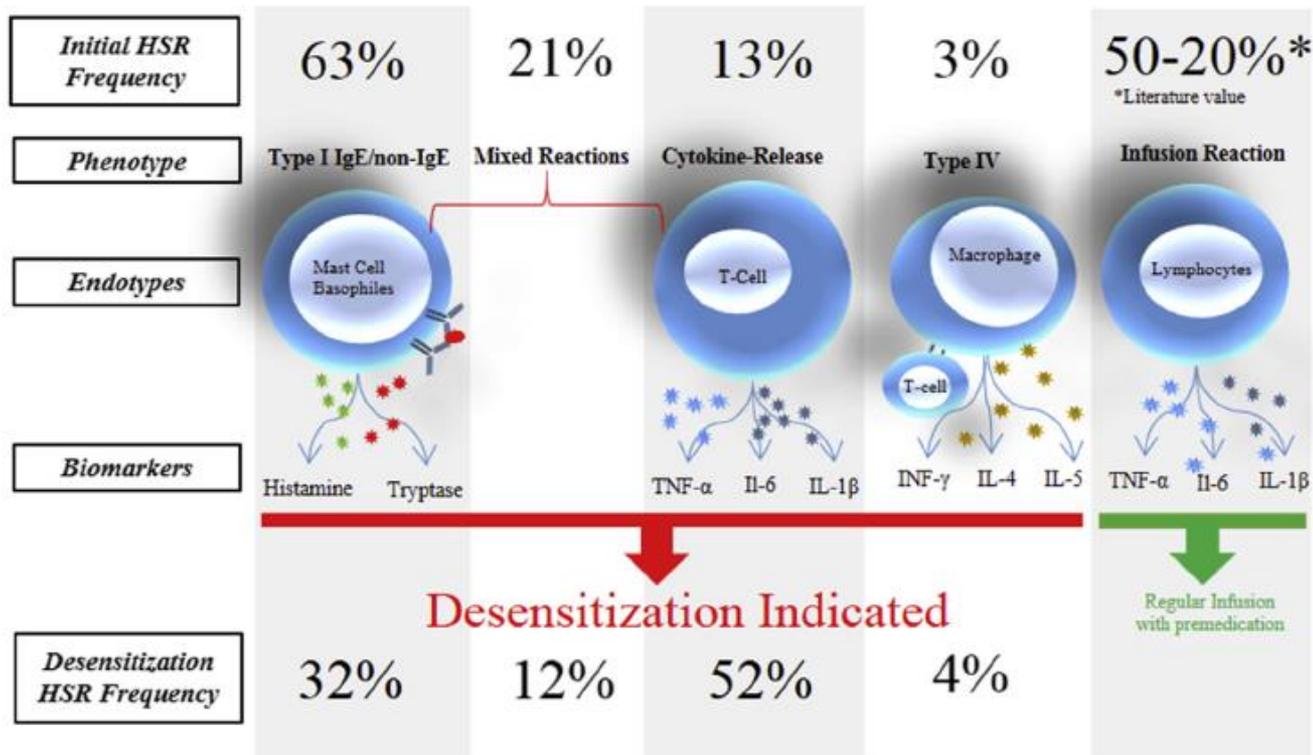
- *Avec un autre sel de platine* : Sept patients de l'enquête ont été traités par un autre sel de platine. Trois d'entre eux ont à nouveau présenté des symptômes d'HS, deux n'ont pas fait de réaction et les autres cas n'ont pas de suivi.

- Tests cutanés : le diagnostic d'hypersensibilité a été confirmé par des tests cutanés chez 3 des 4 patients.

- Les protocoles d'induction de tolérance aux sels de platine consistent en une administration de doses progressivement croissantes jusqu'à une dose cumulée thérapeutique obtenue en plusieurs heures. Cette technique est envisagée lorsque la réaction d'hypersensibilité au médicament constitue une impasse thérapeutique en l'absence d'alternative.

Les anticorps monoclonaux

🚑 Hypersensitivity Reaction to mAbs Precision Medicine Approach



(J Allergy Clin Immunol 2018;142:159-70.)

La désensibilisation

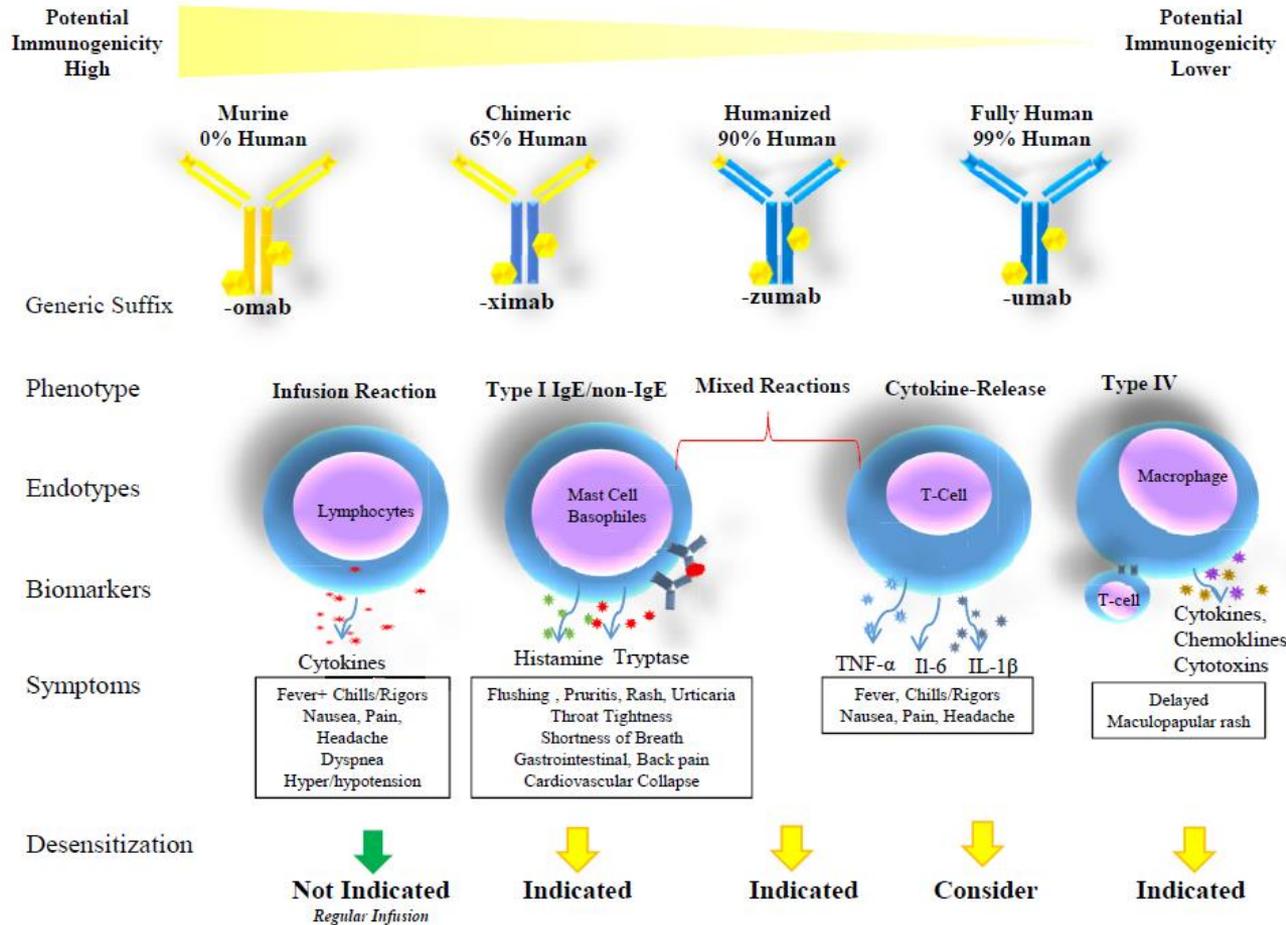


TABLE I. Monoclonal desensitization protocols: Pembrolizumab intravenous desensitization protocol (target dose 200 mg)

Bag	Volume per bag (mL)	Concentration (mg/mL)	Total dose per bag (mg)	Amount of bag infused (mL)
1	100	0.02	2	9.38
2	100	0.2	20	18.75
3	100	1.96063	196.063	100

Step	Bag	Rate (mL/h)	Time (min)	Cumulative time (min)	Volume infused per step (mL)	Dose administered with this step (mg)	Cumulative dose (mg)	Fold increase per step	
1	1	2.5	15	15	0.63	0.0125	0.0125	0	
2	1	5	15	30	1.25	0.025	0.0375	2	
3	1	10	15	45	2.5	0.05	0.0875	2	
4	1	20	15	60	5	0.1	0.1875	2	
5	2	5	15	75	1.25	0.25	0.4375	2.5	
6	2	10	15	90	2.5	0.5	0.9375	2	
7	2	20	15	105	5	1	1.9375	2	
8	2	40	15	120	10	2	3.9375	2	
9	3	10	15	135	2.5	4.9016	8.8391	2.45	
10	3	20	15	150	5	9.8031	18.6422	2	
11	3	40	15	165	10	19.6063	38.2484	2	
12	3	80	61.875	226.88	82.5	161.7516	200		
Total time:				3.78 h					

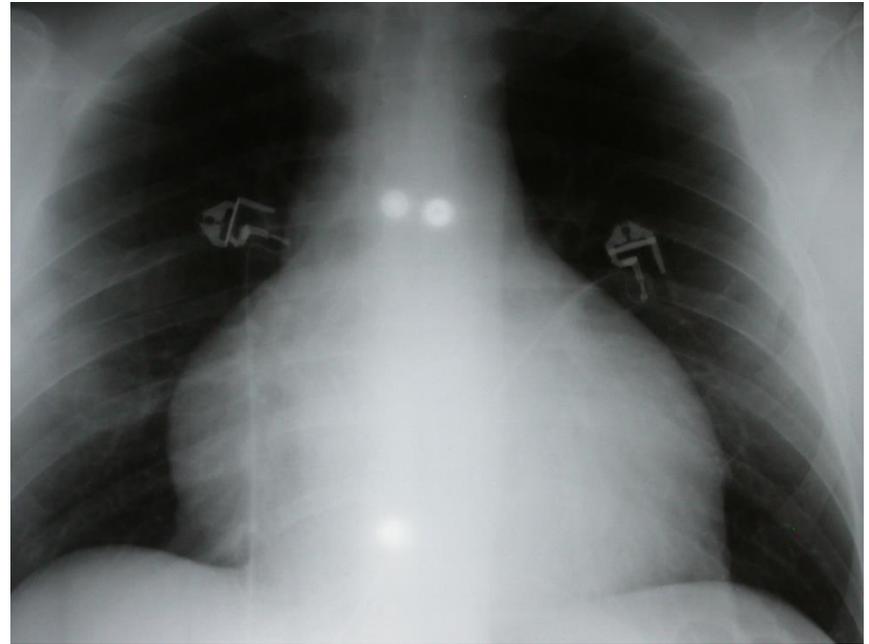
Choc obstructif

=

*obstruction à la circulation du sang
au niveau des grosses veines, du cœur,
des artères pulmonaires, de l'aorte*

Etiologies

- Compression des veines caves
- **tamponnade péricardique**
- ball-valve thrombus, myxome de l'oreillette
- **embolie pulmonaire**
- anévrysme disséquant de l'aorte
- pneumothorax
- *épanchements pleuraux massifs*
- VA à pression positive élevée



Choc cardiogénique

*La pompe cardiaque est incapable
d'assurer un volume circulant suffisant*

Principales étiologies

1. Altérations myocardiques
 - infarctus du myocarde
 - **myocardite aiguë** (sepsis, toxique)
 - cardiomyopathies au stade terminal
2. Lésions valvulaires et septales
 - rupture de pilier ou de cordage tendineux
 - rupture ou perforation valvulaire
 - perforation du septum interventriculaire
3. **Tachycardies** (remplissage diastolique inadéquat)

Choc distributif

déficit majeur de la résistance artérielle et/ ou de la capacité veineuse responsable d'une perturbation de la distribution de la masse sanguine

Contexte de libération de médiateurs de l'inflammation entraînant un état hyperdynamique

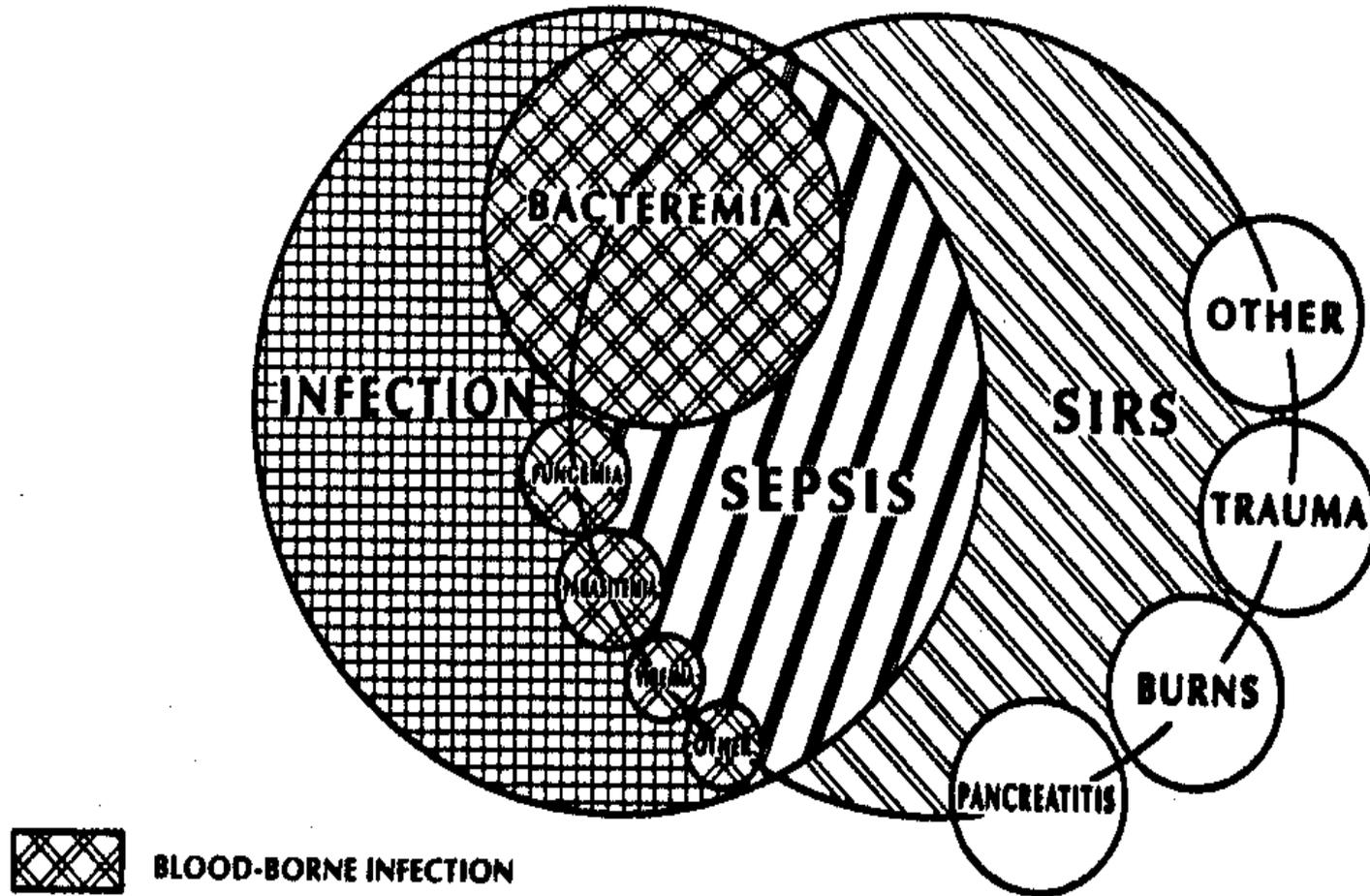


Figure 1. Interrelationships among systemic inflammatory response syndrome (*SIRS*), sepsis, and infection.

La nouvelle définition

= dysfonction d'organe secondaire à une réponse inappropriée de l'hôte envers une infection

- Sepsis
- Choc septique

Sepsis

- si **score SOFA** supérieur ou égal à 2
- ou
- si augmentation supérieure ou égale à 2 points si une dysfonction d'organe est présente avant l'infection

Score SOFA

TABEAU 1

Score SOFA (*Sequential Organ Failure Assessment*)

Organe/Système	Score				
	0	1	2	3	4
↳ Poumons					
PaO ₂ /FiO ₂ mmHg (kPa)	● ≥ 400 (53,3)	● < 400 (53,3)	● < 300 (40)	● < 200 (26,7) avec assistance respiratoire	● ≤ 100 avec assistance respiratoire
↳ Coagulation					
Plaquettes, ×10 ⁹ /L	● ≥ 150	● < 150	● < 100	● < 50	● < 20
↳ Foie					
Bilirubine, mg/dL (μmol/L)	● < 1,2 (20)	● 1,2-1,9 (20-32)	● 2,0-5,9 (33-101)	● 6,0-11,9 (102-204)	● > 12,0 (204)
↳ Cardiovasculaire					
	● PAM ≥ 70 mmHg	● PAM < 70 mmHg	● Dopamine < 5 <i>ou</i> ● Dobutamine	● Dopamine 5,1-15 ● <i>ou</i> Adrénaline ≤ 0,1 ● <i>ou</i> Noradrénaline ≤ 0,1	● Dopamine > 15 ● <i>ou</i> Adrénaline > 0,1 ● <i>ou</i> Noradrénaline > 0,1
↳ Système nerveux central					
Score de Glasgow	● 15	● 13-14	● 10-12	● 6-9	● < 6
↳ Rein					
Créatinine, mg/dL (μmol/L)	● < 1,2 (110)	● 1,2-1,9 (110-170)	● 2,0-3,4 (171-299)	● 3,5-4,9 (300-440)	● > 5,0 (440)
Diurèse, mL/j				● < 500	● < 200

PaO₂ : pression artérielle en oxygène ; FiO₂ : fraction d'oxygène inspiré ; PAM : pression artérielle moyenne. La dose de catécholamines est donnée en μg/kg/min sur au moins 1 heure.

Choc septique

- défini par l'association d'un **sepsis**, de la nécessité de médicaments **vasopresseurs** pour maintenir une pression artérielle moyenne supérieure ou égale à 65 mm Hg et un taux de **lactate** supérieur à 2 mmol/L malgré un remplissage adéquat.

Dépistage du sepsis

La présence d'au moins deux critères sur trois justifie une surveillance accrue et/ou un traitement spécifique en réanimation

TABEAU 2	Quick SOFA	
Quick SOFA (≥ 2 critères) :		
● FR ≥ 22/min	● Glasgow ≤ 13	● PAS ≤ 100 mmHg

**Cette nouvelle définition a été validée dans
deux études spécifiques aux soins intensifs
oncologiques.**



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Accuracy of SOFA, qSOFA, and SIRS scores for mortality in cancer patients admitted to an intensive care unit with suspected infection☆



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Table 2
Performance of SIRS, qSOFA and SOFA criteria for prediction of ICU and hospital mortality.

	ICU mortality			Hospital mortality		
	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
SIRS	68.0 (62.1–73.5)	52 (44.3–59.6)	0.62 (0.56–0.67)	67.6 (60.3–74.2)	44.9 (38.8–51.1)	0.58 (0.52–0.63)
qSOFA	78.3 (71.3–84.3)	52.8 (46.6–58.9)	0.71 (0.65–0.76)	72.5 (66.5–77.9)	59.3 (51.8–66.5)	0.69 (0.64–0.74)
SOFA	96.4 (92.7–98.7)	13.1 (9.3–17.7)	0.76 (0.71–0.81)	95.1 (91.7–97.4)	15.7 (10.8–21.7)	0.69 (0.65–0.74)

AUC: area under the receiver operating characteristic curve, CI: confidence interval, ICU: intensive care unit, SIRS: systemic inflammatory response syndrome, SOFA: sequential organ failure assessment.

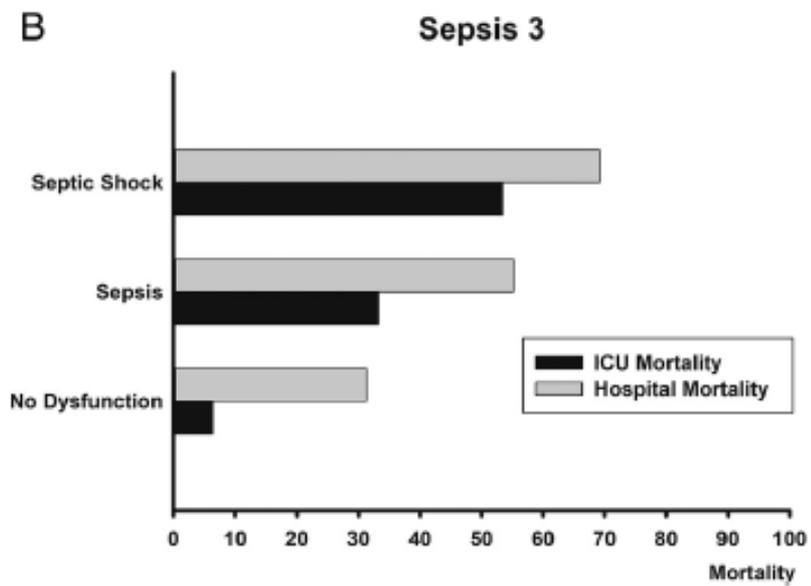
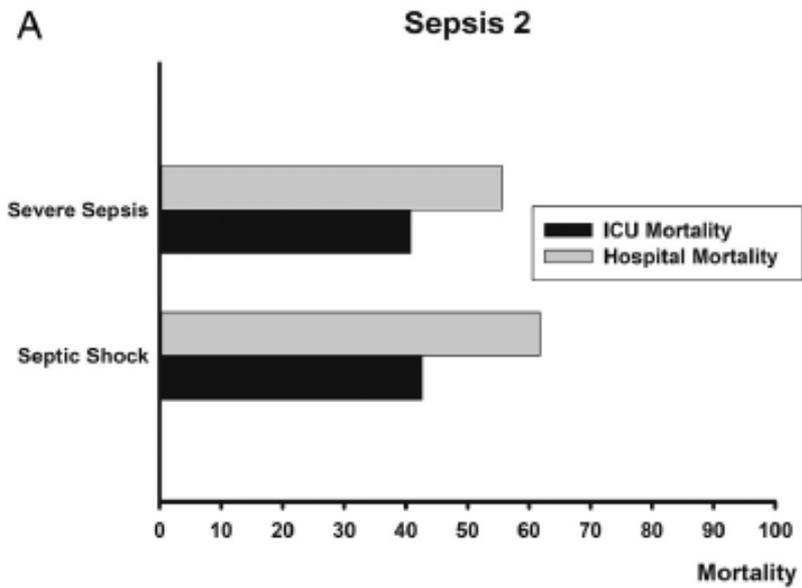


Fig. 2. Mortality across Sepsis-2 (a) and Sepsis-3 (b) definitions.

Sepsis and Septic Shock Definitions in Patients With Cancer Admitted in ICU

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Table 4. Comparison of Old and New Definitions of Sepsis and Septic Shock.

Sepsis Gravity	Old Definition		New Definition	
	Alive at Hospital Discharge	In-Hospital Death	Alive at Hospital Discharge	In-Hospital Death
Sepsis	9		267	
	8 (89%)	1 (11%)	180 (67%)	87 (33%)
Severe sepsis	271		/	
	185 (68%)	86 (32%)		
Septic shock	68		57	
	27 (40%)	41 (60%)	18 (32%)	39 (68%)

Table 5. Comparison of AUROCs for SOFA, qSOFA, and SIRS Criteria for Predicting In-Hospital Mortality.

Studies	AUROC SOFA	AUROC qSOFA	AUROC SIRS
Seymour et al ³	0.74	0.66	0.64
Raith et al ⁴	0.75	0.61	0.59
Costa et al ⁵	0.69	0.69	0.58
This study	0.74 (95% CI, 0.68-0.79)	0.65 (95% CI, 0.59-0.70)	0.58 (95% CI, 0.52-0.63)

Abbreviations: AUROC, areas under ROC curve; CI, confidence interval; qSOFA, quick Sequential Organ Failure Assessment; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment.

Données spécifiques

- Neutropénie de mauvaise réputation chez le cancéreux
 - neutropénie fébrile: 1^{ère} cause de mort infectieuse (12/19 cas)
 - mortalité de 82% (18/22) dans une contexte de neutropénie fébrile
 - la neutropénie ne protège pas contre la survenue d'un SDRA et d'un syndrome de défaillance multiviscérale
- A traiter au moindre doute par une antibiothérapie empirique jusqu'à obtention d'une documentation microbiologique avec support ordinaire de réanimation (expandeurs, cathécolamines, VM)

Choix initial

- **sepsis sans foyer** : une β -lactamine à large spectre (céphalosporine ou carbapénem : imipénem-cilastatine ou méropénem) + aminoside (amikacine) : 15 mg/kg 1 x/j (DT 1,5 g/j)
- **infections abdominales pelviennes** (anaérobies) : imipénem-cilastatine ou pipéracilline-tazobactam ou méropénem + aminoside
- **suspicion d'infection à staphylocoque** : β -lactamine à large spectre + vancomycine (2 x 1 g i.v.)
- **neutropénie fébrile** : céphalosporine ou imipénem-cilastatine ou pipéracilline-tazobactam + amikacine

Amélioration du pronostic

Importance de l'expérience clinique

Impact of case volume on survival of septic shock in patients with malignancies*

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(Crit Care Med 2012; 40:55–62)

Table 1. Characteristics of patients and differences between survivors and nonsurvivors

Patient Characteristics	Patients (n = 3437)	Survivors (n = 1408)	Deceased (n = 2029)	Odds Ratio (95% Confidence Interval)	<i>p</i>
Age, years	62.2 ± 14.3	60.0 ± 14.6	63.6 ± 13.9	1.016 [1.011–1.021]	<.001
Gender, male	2242 (65.2%)	922 (65.4%)	1320 (65.1%)	1.030 [0.888–1.194]	.70
Type of admission, direct	1176 (34.2%)	490 (34.8%)	686 (33.8%)	0.958 [0.825–1.114]	.57
Admission category, medical	2720 (79.1%)	1080 (76.7%)	1640 (80.8%)	1.424 [1.186–1.710]	<.001
Type of malignancy					
Hematologic malignancy	1318 (38.3%)	502 (35.7%)	816 (40.2%)	1.373 [1.175–1.605]	<.001
Solid tumor	2119 (61.6%)	906 (64.3%)	1213 (59.8%)		
Neutropenia	871 (25.3%)	339 (24.1%)	532 (26.2%)	1.174 [0.995–1.385]	.06
Comorbidities					
Diabetes mellitus	170 (4.9%)	61 (4.3%)	109 (5.4%)	1.254 [0.909–1.017]	.02
Chronic pulmonary disease	319 (9.3%)	118 (8.4%)	201 (9.9%)	1.202 [0.947–1.525]	.13
Chronic heart failure	55 (1.6%)	20 (1.4%)	35 (1.7%)	1.218 [0.700–2.119]	.48
Chronic renal insufficiency	130 (3.8%)	51 (3.6%)	79 (3.9%)	1.077 [0.735–1.542]	.68
Cirrhosis	147 (4.2%)	45 (3.2%)	102 (5.0%)	1.603 [1.121–2.292]	.01
Simplified Acute Physiology Score II, points	63.4 ± 25.1	50.8 ± 17.2	72.1 ± 26.0	1.045 [1.040–1.049]	<.001
Site of infection					
Lung	1212 (49.3%)	457 (46.9%)	755 (50.8%)	1.250 [1.076–1.453]	.005
Abdominal	372 (15.1%)	163 (16.7%)	209 (14.1%)	0.828 [0.659–1.040]	.11
Urinary tract	171 (6.9%)	98 (10.1%)	73 (4.9%)	0.510 [0.370–0.703]	<.001
Others	197 (8.0%)	83 (8.5%)	114 (7.7%)	0.969 [0.713–1.318]	.22
Unknown	508 (20.6%)	173 (17.8%)	335 (22.5%)	1.472 [1.191–1.820]	<.001
Positive blood culture	1633 (47.5%)	729 (51.8%)	904 (44.6%)	0.750 [0.648–0.868]	<.001
Type of microorganisms					
Bacteria	1885 (55.9%)	839 (59.6%)	1046 (51.6%)	0.733 [0.635–0.847]	<.001
Gram-negative	1174 (34.2%)	512 (36.4%)	662 (32.6%)	0.841 [0.720–0.981]	.03
Gram-positive	859 (25.0%)	363 (25.8%)	496 (24.4%)	0.949 [0.775–1.163]	.11
Fungus	247 (7.2%)	82 (5.8%)	165 (8.1%)	1.526 [1.148–2.028]	.006
Parasite	36 (1.0%)	11 (0.8%)	25 (1.2%)	1.689 [0.808–3.531]	.16
Virus	54 (1.6%)	28 (2.0%)	26 (1.3%)	0.704 [0.403–1.229]	.21
Unknown	1430 (41.6%)	530 (37.6%)	900 (44.4%)	1.279 [1.105–1.481]	.002
Circulatory support	2961 (86.2%)	1092 (77.6%)	1869 (92.1%)	3.500 [2.826–4.334]	<.001
Invasive mechanical ventilation	2635 (76.7%)	779 (55.3%)	1856 (91.5%)	9.149 [7.504–11.153]	<.001
Renal replacement therapy	864 (25.1%)	186 (13.2%)	678 (33.4%)	3.527 [2.920–4.260]	<.001

Variables are reported as mean ± SD (continuous variables) or number and percentages (categorical variables), and are compared by hierarchical regression between survivors and nonsurvivors.

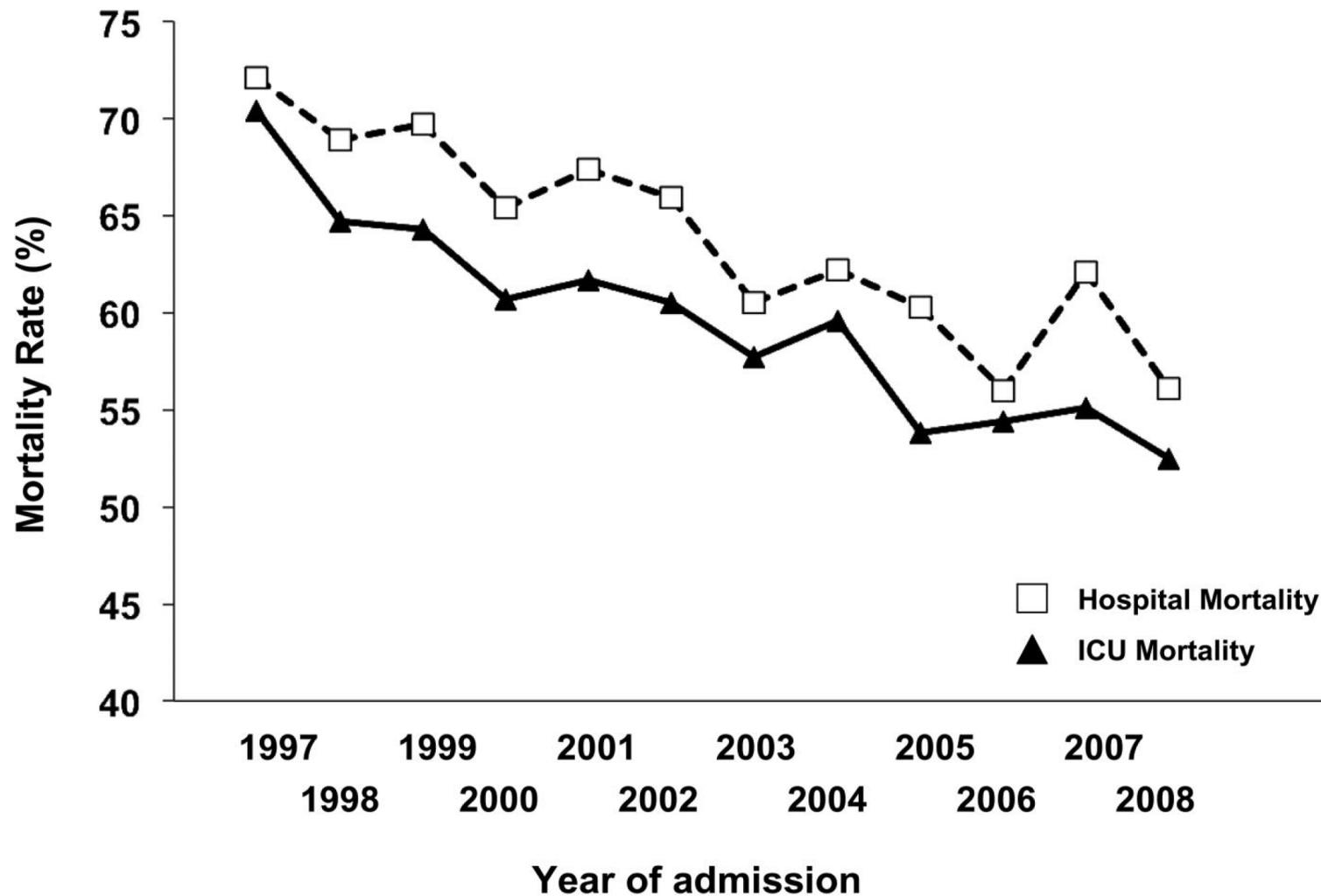


Figure 1. Intensive care unit (ICU) and hospital outcomes between 1997 and 2008. Chi-square test for trend over the study period for ICU and hospital mortality: $p < .001$

Low: < 5 cas/an; High : > 13 cas/an

Table 2. Characteristics of units and admissions within volume tertiles

Admission Characteristics	Low-Volume Tertile (n = 299)	Medium-Volume Tertile (n = 788)	High-Volume Tertile (n = 2350)	<i>p</i>
Annual number of ICU admissions	407.0 ± 142.8	467.6 ± 182	613.3 ± 235.9	<.001
Annual number of septic shock patients	19.6 ± 13.7	37.7 ± 17.7	76.9 ± 27.2	<.001
Annual number of septic shock cancer patients	2.8 ± 1.1	8.2 ± 2.3	23.6 ± 13.6	<.001
Age, years	64.0 ± 13.6	64.4 ± 13.5	61.24 ± 14.6	<.001
Age, >80	12.0	10.1	7.9	.005
Gender, male	68.2	67.6	64.0	.03
Comorbidities				
Diabetes mellitus	5.3	5.2	4.8	.58
Chronic pulmonary disease	8.0	9.0	9.3	.42
Chronic heart failure	0.3	1.2	1.8	.05
Chronic renal insufficiency	3.3	3.9	3.7	.92
Cirrhosis	4.6	4.8	4.0	.34
University hospital	56.9	64.3	92.7	<.001
Type of admission, direct	41.5	33.9	33.4	.06
Admission category, medical	78.3	78.8	79.4	.88
Specialized wards in hospital				
Hematology and oncology wards	42	52.6	75.5	<.001
Hematology or oncology ward	13.4	12.6	8.5	.08
No specialized ward	44.5	34.8	16.0	<.001
Type of malignancy				
Hematologic malignancy	28.4	28.4	42.9	<.001
Solid tumor	71.6	71.6	57.1	<.001
Neutropenia	21.7	23.9	26.3	.04
Simplified Acute Physiology Score II, points	63.4 ± 24.5	64.8 ± 24.7	63.0 ± 25.4	.21
Circulatory support	83.6	86.9	86.2	.36
Invasive mechanical ventilation	76.9	75.9	76.9	.84
Renal replacement therapy	19.4	25.5	26.2	.06
Length of ICU stay, days	12.7 ± 17.9	11.6 ± 15.1	12.1 ± 15.3	.99
ICU mortality	64.9	61.0	57.6	.05

ICU, intensive care unit. Variables are reported as mean ± SD (continuous variables) or percentages (categorical variables).

Table 3. Prognostic factors of intensive care unit mortality: results of the multivariate conditional logistic regression analysis after matching on the propensity score and on the year of admission

Variable	Odds Ratio (95% Confidence Interval)	<i>p</i>
Admission category, medical	1.73 [1.29–2.32]	<.001
Simplified Acute Physiology Score II (per point)	1.036 [1.03–1.04]	<.001
Invasive mechanical ventilation	5.52 [4.04–7.54]	<.001
Renal replacement therapy	1.74 [1.30–2.33]	.001
Fungal infection	1.95 [1.18–3.21]	.009
Microorganism unknown	1.64 [1.27–2.11]	<.001
Admission to medium- vs. low-volume unit	0.82 [0.59–1.14]	.78
Admission to high- vs. low-volume unit	0.63 [0.46–0.87]	.002

The goodness-of-fit of the model was checked by the Akaike information criterion.

Amélioration du pronostic au cours des années

Sepsis and Septic Shock in Patients With Malignancies: A Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique Study*

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Edith Borcoman, MD¹; Magali Bisbal, MD³; Matthieu Legrand, MD, PhD¹; Dominique Benoit, MD, PhD¹⁰;
Elie Azoulay, MD, PhD¹; Michaël Darmon, MD, PhD¹; Lara Zafrani, MD, PhD^{1,2}

Objectives: Cancer affects up to 20% of critically ill patients, and sepsis is one of the leading reasons for ICU admission in this setting. Early signals suggested that survival might be increasing in this population. However, confirmation studies have been lacking. The goal of this study was to assess trends in survival rates over time in cancer patients admitted to the ICU for sepsis or septic shock over the last 2 decades.

Data Source: Seven European ICUs.

22.3%), and myeloma ($n = 244$; 11.8%). Two-hundred fifty patients (12%) underwent allogeneic hematopoietic stem cell transplantation and 640 (31.0%) were neutropenic at ICU admission. Day 30 mortality was 39.9% (823 deaths). The year of ICU admission was associated with significant decrease in day 30 mortality over time (odds ratio, 0.96; 95% CI, 0.93–0.98; $p = 0.001$). Mechanical ventilation (odds ratio, 3.25; 95% CI, 2.52–4.19; $p < 0.01$) and vasopressors use (odds ratio, 1.42; 95% CI, 1.10–1.83; $p < 0.01$) were

TABLE 1. Population Characteristics According to Day 30 Outcome

Variables	All (<i>n</i> = 2,062)	Survivors at Day 30 (<i>n</i> = 1,205)	Nonsurvivors at Day 30 (<i>n</i> = 823)	Univariate Analysis <i>p</i>
Gender, female, <i>n</i> (%)	787 (38.1)	465 (38.6)	322 (39.1)	1.00
Age, yr, median (IQR)	59 (48–67)	59 (47–67)	59 (49–68)	0.52
Year of inclusion, median (IQR)	2009 (2006–2010)	2010 (2007–2011)	2009 (2006–2010)	< 0.01
Sequential Organ Failure Assessment score at ICU admission, median (IQR)	6 (4–9)	6 (4–9)	8 (5–11)	< 0.01
Comorbidities, <i>n</i> (%)	1,043 (50.6)	645 (53.5)	398 (48.4)	0.41
Hematologic malignancies, <i>n</i> (%)	1,700 (82.4)	986 (81.8)	685 (83.2)	0.45
Allogeneic stem cell transplantation, <i>n</i> (%)	250 (12.1)	151 (12.5)	99 (12.0)	0.92
Neutropenia, <i>n</i> (%)	640 (31.0)	365 (30.3)	275 (33.4)	0.09
Acute respiratory failure, <i>n</i> (%)	927 (45.0)	578 (48.0)	349 (46.0)	0.50
Noninvasive ventilation, <i>n</i> (%)	635 (30.8)	357 (29.6)	278 (33.8)	0.05
Mechanical ventilation, <i>n</i> (%)	1,016 (49.3)	423 (35.1)	593 (72.0)	< 0.01
Vasopressor use, <i>n</i> (%)	1,172 (56.8)	577 (47.9)	595 (72.3)	< 0.01
Acute kidney injury, <i>n</i> (%)	291 (14.1)	173 (14.4)	118 (14.3)	0.31
Renal replacement therapy, <i>n</i> (%)	420 (20.4)	182 (15.1)	238 (28.9)	< 0.01

IQR = interquartile range.

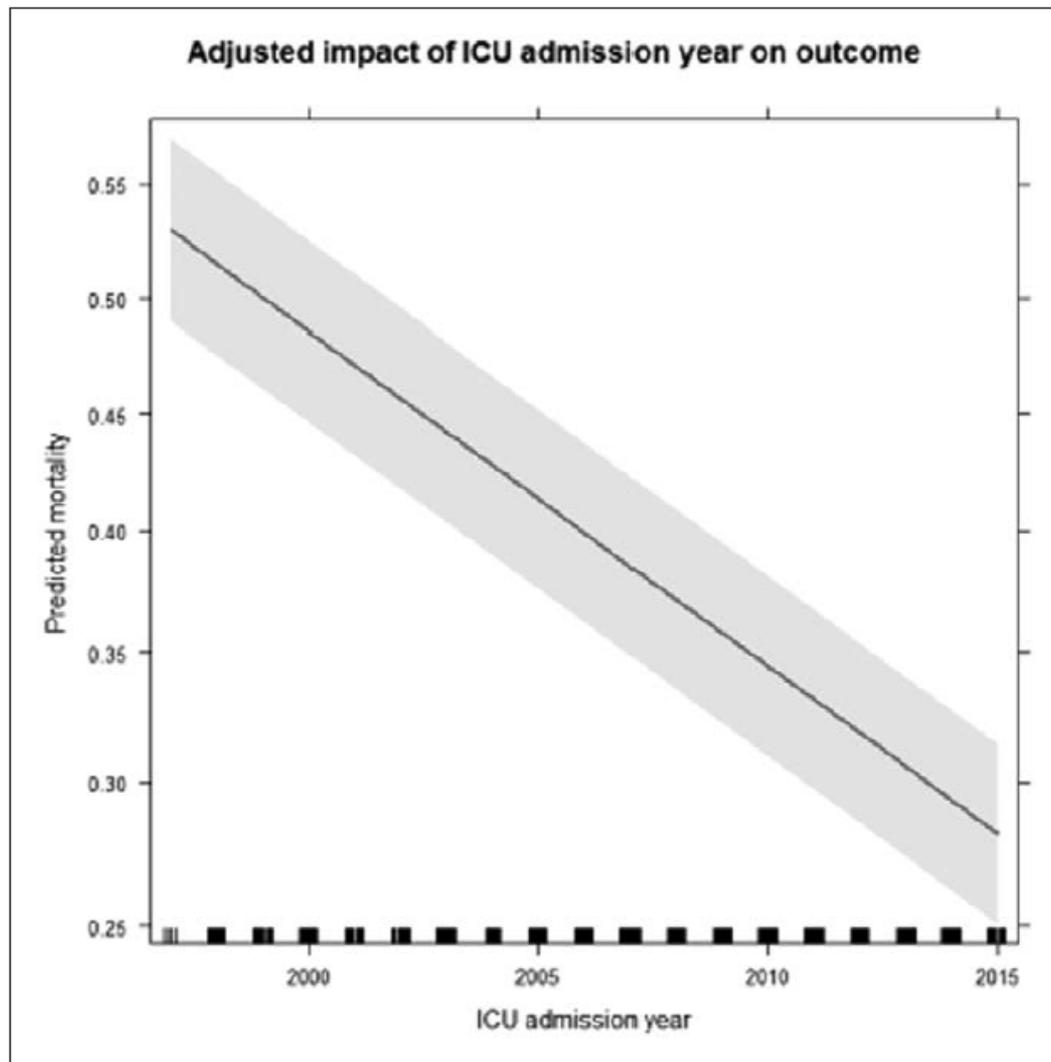


Figure 1. Thirty-day predicted mortality obtained by mixed-effect linear regression according to the year of ICU admission and adjusted on Sequential Organ Failure Assessment score at ICU admission.

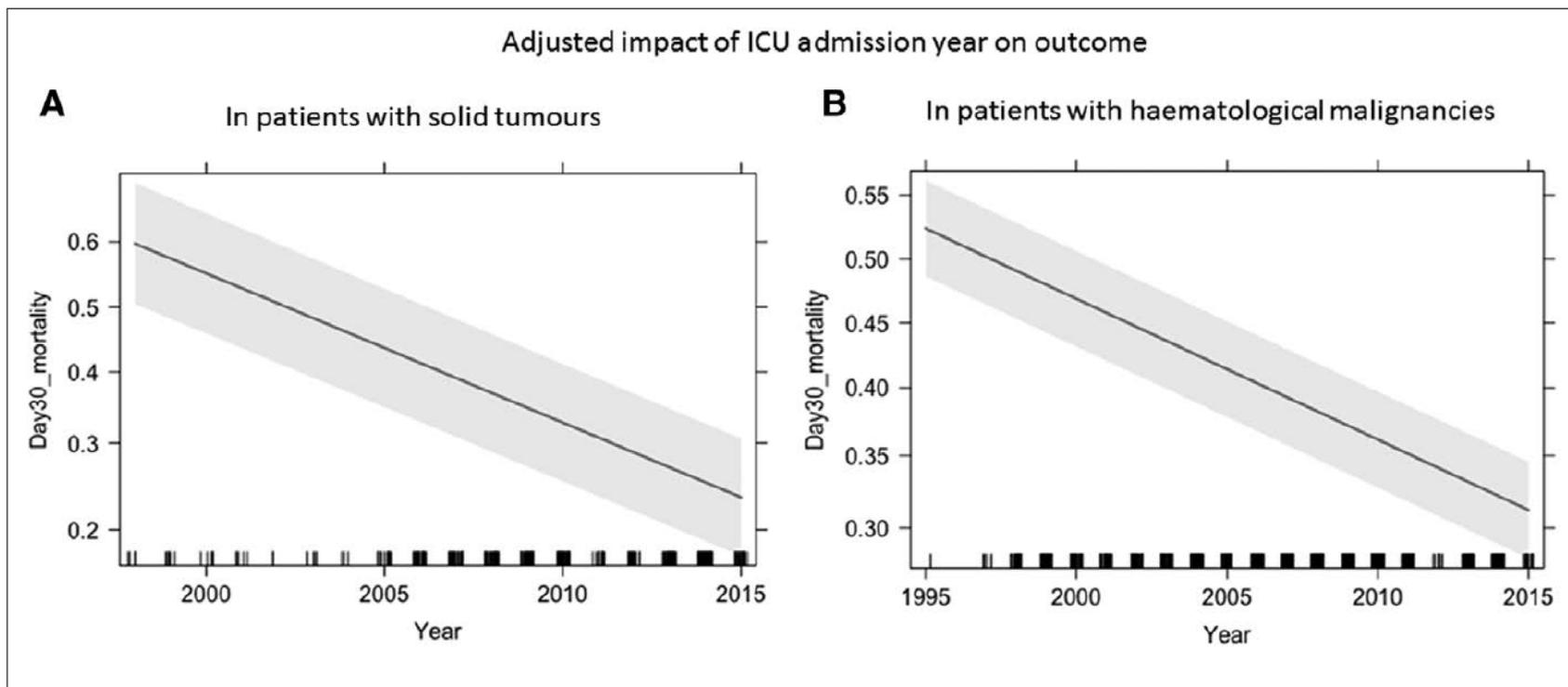


Figure 2. Thirty-day mortality over the years according the type of tumor. Thirty-day predicted mortality obtained by mixed-effect linear regression according to the year of ICU admission and adjusted on Sequential Organ Failure Assessment score at ICU admission in **(A)** patients with solid tumors **(B)** patients with hematologic malignancies.

Amélioration aussi de la survie chez le neutropénique

Survival in neutropenic patients with severe sepsis or septic shock*

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Objective: To determine whether the survival gains achieved in critically ill cancer patients in recent years exist in the subset with neutropenia and severe sepsis or septic shock.

Design: Retrospective 11-yr study (1998–2008).

Setting: Medical intensive care unit in a teaching hospital.

Patients: Four hundred twenty-eight intensive care unit patients with cancer, neutropenia, and severe sepsis or septic shock. The primary outcome was hospital mortality.

Results: The main underlying diseases were acute leukemia (35.7%), lymphoma (31.7%), and solid tumors (16.5%). Two hundred thirty-seven (55.5%) patients had microbiologically documented infections, 141 (32.9%) clinically documented infections, and 50 (11.9%) fever of unknown origin. Acute noninfectious conditions were diagnosed in 175 of 428 (41%) patients, including 26 of 50 (52%) patients with fever of unknown origin, 66 of 141 (47%) patients with clinically documented infections, and 83 of 237 (35%) patients with microbiologically documented infections. Early indwelling catheter removal was performed routinely in the 107 (25%) patients without clinical evidence of a septic focus at intensive care unit

admission. Early beta-lactam plus aminoglycoside therapy was used in 391 (91.3%) patients. Hospital mortality was 49.8%. Hospital mortality decreased from 58.7% (108 of 184) in 1998–2003 to 43% in 2004–2008 (105 of 244, $p = .006$). Multivariate analysis identified nine independent predictors of hospital mortality, of which six were associated with higher mortality (older age; need for vasopressors; neurologic, respiratory, or hepatic dysfunction; and acute noninfectious condition) and three with lower mortality (intensive care unit admission after 2003, combination antibiotic therapy including an aminoglycoside, and early indwelling catheter removal).

Conclusion: In neutropenic patients with severe sepsis or septic shock, survival improved over time. Aminoglycoside use and early catheter removal in patients with undocumented sepsis may improve survival. Acute noninfectious conditions are associated with increased mortality, underlining the need for thorough and repeated clinical assessments. (Crit Care Med 2012; 40: 43–49)

KEY WORDS: diagnosis; management; neutropenia; outcomes; sepsis; shock

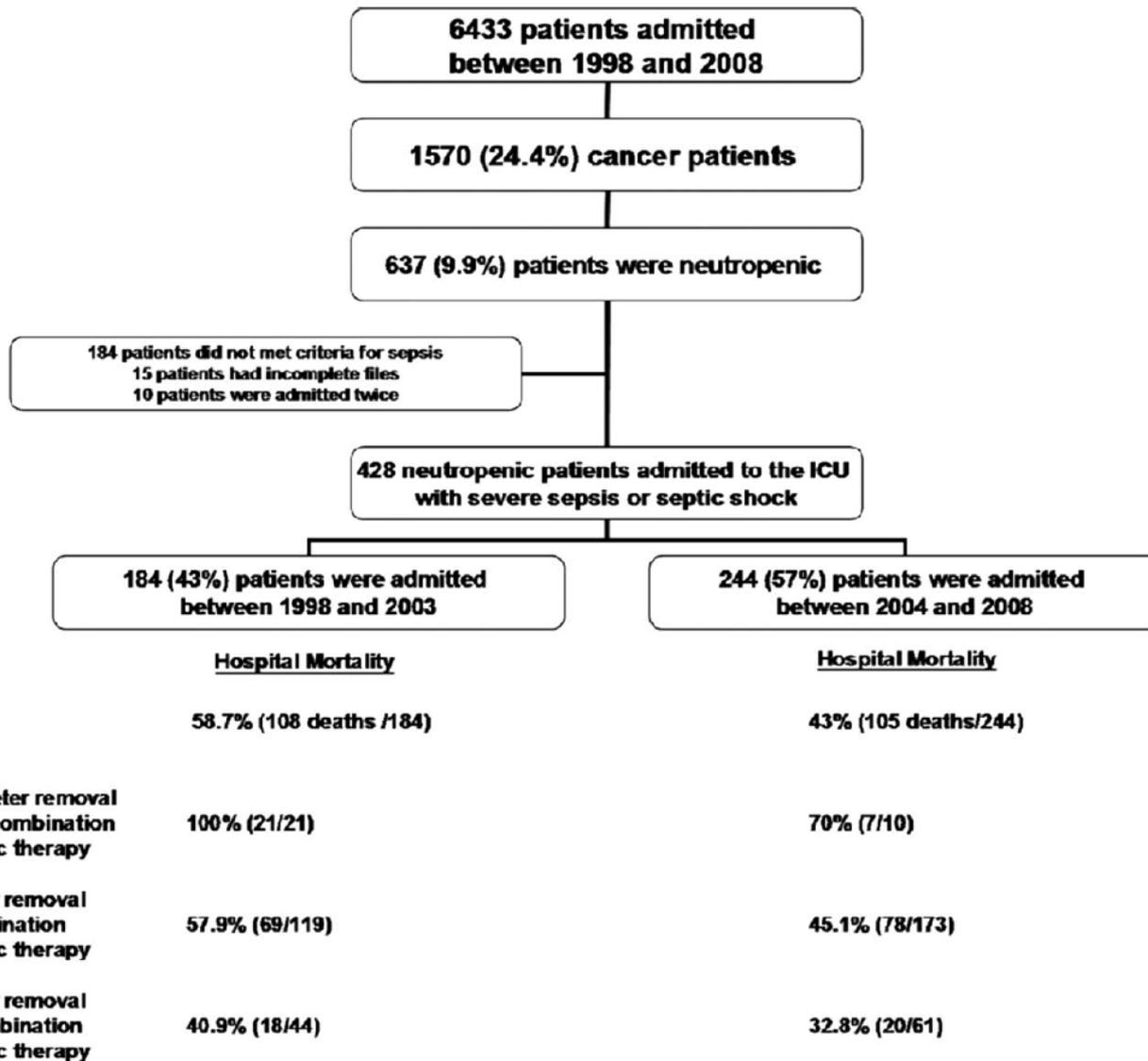


Figure 1. Flow chart of patients admitted to our medical intensive care unit (ICU) between 1998 and 2008.

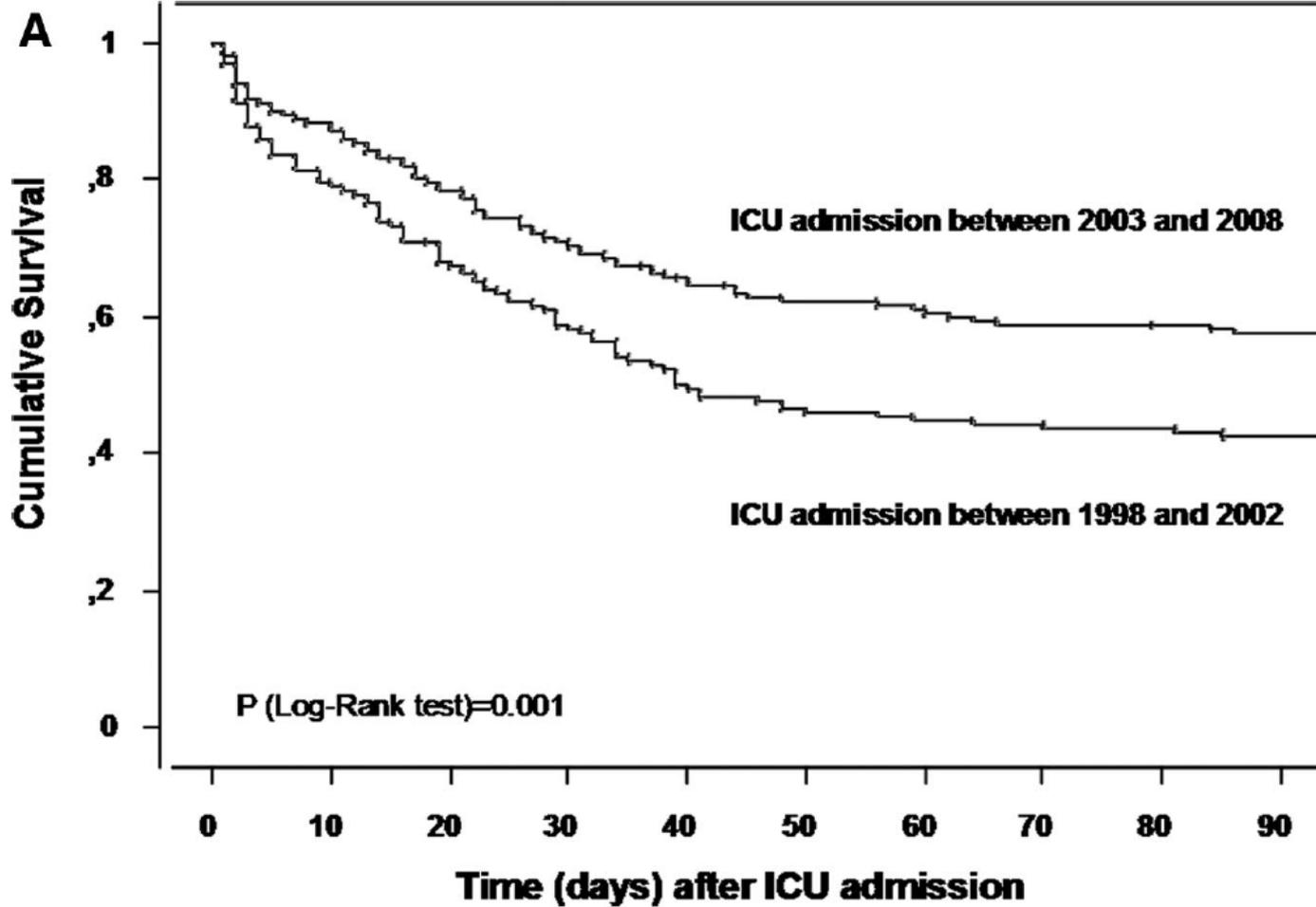


Table 5. Multivariate analysis of factors associated with in-hospital mortality

Variable, N (%) or Median (25th–75th)	Alive (n = 215)	Dead (n = 213)	Odds Ratio (95% Confidence Interval)	<i>p</i>
Age, yrs	47 (35–57)	54 (43–65)	1.036 (1.02–1.05)	<.0001
Intensive care unit admission during the second period (between 2004 and 2008)	139 (64.6)	105 (49.3)	0.56 (0.36–0.89)	.01
Shock	123 (57.2)	181 (85.0)	2.69 (1.65–4.38)	<.0001
Acute respiratory failure	61 (28.4)	171 (80.3)	1.98 (1.14–3.44)	.015
Neurologic failure	7 (3.2)	37 (17.4)	4.03 (1.03–15.8)	.04
Hepatic failure	7 (3.2)	20 (9.4)	1.49 (1.16–1.91)	.002
Early acute noninfectious conditions	77 (35.8)	98 (46.0)	1.69 (1.06–2.68)	.02
Initial combination antibiotic therapy	210 (97.7)	181 (85.0)	0.164 (0.05–0.51)	.002
Indwelling catheter removal	68 (31.6)	39 (18.3)	0.50 (0.30–0.85)	.01

Goodness of fit (Hosmer-Lemeshow) chi-square *p* value = .64. Area under the receiver operating characteristic curve = .74.

La chimiothérapie récente n'obtempère pas le pronostic

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ORIGINAL

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**Impact of recent intravenous chemotherapy
on outcome in severe sepsis and septic shock
patients with hematological malignancies**

Table 4 Severity of illness and outcome of 186 critically ill patients with hematological malignancies who did vs. who did not receive recent chemotherapy (CHT) (APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; CSSIS, Cancer Specific Severity of Illness Score; DNR, do not resuscitate; IQR, interquartile range)

	CHT (<i>n</i> = 91)	No CHT (<i>n</i> = 95)	<i>p</i>
Severity of illness upon admission			
APACHE II (points)	25.3±6.8	26.9±6.9	0.094
SOFA (points)	9.7±3.5	10.4±4.0	0.231
CSSIS (probability of hospital death)	77.2±20.4	78.6±21.4	0.473
Ventilation	45 (49.5%)	61 (64.2%)	0.054
PaO ₂ /FIO ₂	206.9±139.8	152.2±96.3	0.022
Hemodynamics			
Severe sepsis	41 (41.4%)	36 (37.9%)	0.372
Septic shock	50 (54.9%)	59 (62.1%)	
Noradrenaline dose (ng kg ⁻¹ min ⁻¹)	207±374	298±523	0.358
Severity of illness during ICU stay			
Ventilation	52 (57.1%)	69 (72.6%)	0.041
Noninvasive ventilation	9 (9.9%)	14 (14.7%)	0.376
Invasive mechanical ventilation	43 (47.3%)	55 (57.9%)	0.186
Renal replacement therapy	14 (15.4%)	26 (27.4%)	0.130
Length of stay (days; IQR)	5.0 (3.0–13.0)	7.0 (4.0–11.3)	0.326
Outcome			
DNR order	27 (29.7%)	35 (38.0)	0.275
Days until DNR order ^a	4.0 (3.0–13.0)	6.0 (3.0–11.0)	0.679
ICU mortality	30 (33.0)	46 (48.4)	0.037
28-day mortality	37 (40.7)	54 (57.4)	0.027
In-hospital mortality	41 (45.1)	56 (58.9)	0.076
6-month mortality	46 (50.5)	60 (63.2)	0.103

^aWithin the subgroup of patients with DNR options

Table 5 Impact of previous intravenous chemotherapy on 28-day mortality after adjustment for potential confounders present before and upon ICU admission (*OR*, odds ratio; *CI*, confidence interval;

SOFA, Sequential Organ Failure Assessment; *ROC*, receiver operating characteristics curve)

	OR	95% CI	<i>p</i>
Unadjusted			
Intravenous chemotherapy	0.51	0.28–0.911	0.023
Adjusted for variables before ICU admission^a			
Intravenous chemotherapy	0.35	0.16–0.75	0.007
Age (per year)	1.01	0.99–1.03	0.295
High-grade malignancy	1.22	0.60–2.51	0.586
Active disease	2.11	1.09–4.06	0.026
Combination antibiotic therapy	2.54	1.24–5.22	0.011
Neutropenia	1.09	0.53–2.25	0.812
Days of hospitalization (per day)	0.99	0.97–1.01	0.432
Adjusted for variables upon ICU admission and the most important variables before admission^b			
Intravenous chemotherapy	0.48	0.23–1.00	0.049
Active disease	1.98	0.95–4.14	0.069
Combination of antibiotic therapy	1.52	0.71–3.23	0.280
Pulmonary site of infection	2.84	1.38–5.84	0.005
Fungal infection	4.18	1.61–10.87	0.003
SOFA (per point)	1.26	1.14–1.39	< 0.001
Additionally adjusted for propensity score^c			
Intravenous chemotherapy	0.50	0.23–1.08	0.079
Active disease	1.76	0.80–3.84	0.158
Combination of antibiotic therapy	1.51	0.65–3.49	0.341
Pulmonary site of infection	2.85	1.39–7.57	0.009
Fungal infection	4.04	1.50–10.83	0.006
SOFA (per point)	1.28	1.15–1.42	< 0.001
Propensity score	1.52	0.18–12.68	0.697

^aHosmer and Lemeshow: $\chi^2 = 9.04$, *df* 8, *p* = 0.34, ROC 0.68 (0.60–0.75), SE = 0.039; ^bHosmer and Lemeshow: $\chi^2 = 6.07$, *df* 8, *p* = 0.64, ROC 0.82 (0.74–0.87), SE = 0.032; ^cHosmer and Lemeshow: $\chi^2 = 3.42$, *df* 8, *p* = 0.91, ROC 0.81 (0.75–0.87), SE = 0.032

La mortalité est significativement plus élevée dans les transplantations allogéniques et en cas de maladie du greffon contre l'hôte

Severe Sepsis in Hematopoietic Stem Cell Transplant Recipients*

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Objective: Severe sepsis requires timely management and has high mortality if care is delayed. Hematopoietic stem cell transplant recipients are more likely to be immunocompromised and are predisposed to serious infections. Reports of outcomes of severe sepsis in this population are limited to data from single, tertiary care centers, and national outcomes data are missing.

Design: Retrospective analysis of an administrative database.

Setting: Twenty percent of community hospitals in United States, excluding federal hospitals.

Subject: Patients with severe sepsis.

mixed effect, multivariate logistic regression modeling with propensity score adjustment to examine factors associated with mortality of severe sepsis in hematopoietic stem cell transplant recipients. A total of 21,898 hematopoietic stem cell transplant recipients with severe sepsis were identified. The frequency of severe sepsis in hematopoietic stem cell transplant recipients was five times higher when compared with the non-hematopoietic stem cell transplant cohort. The unadjusted mortality was 32.9% in non-hematopoietic stem cell transplant cohort, which was similar to autologous hematopoietic stem cell transplant recipients (30.1%) and those who did not (*Crit Care Med* 2015; 43:411–421)

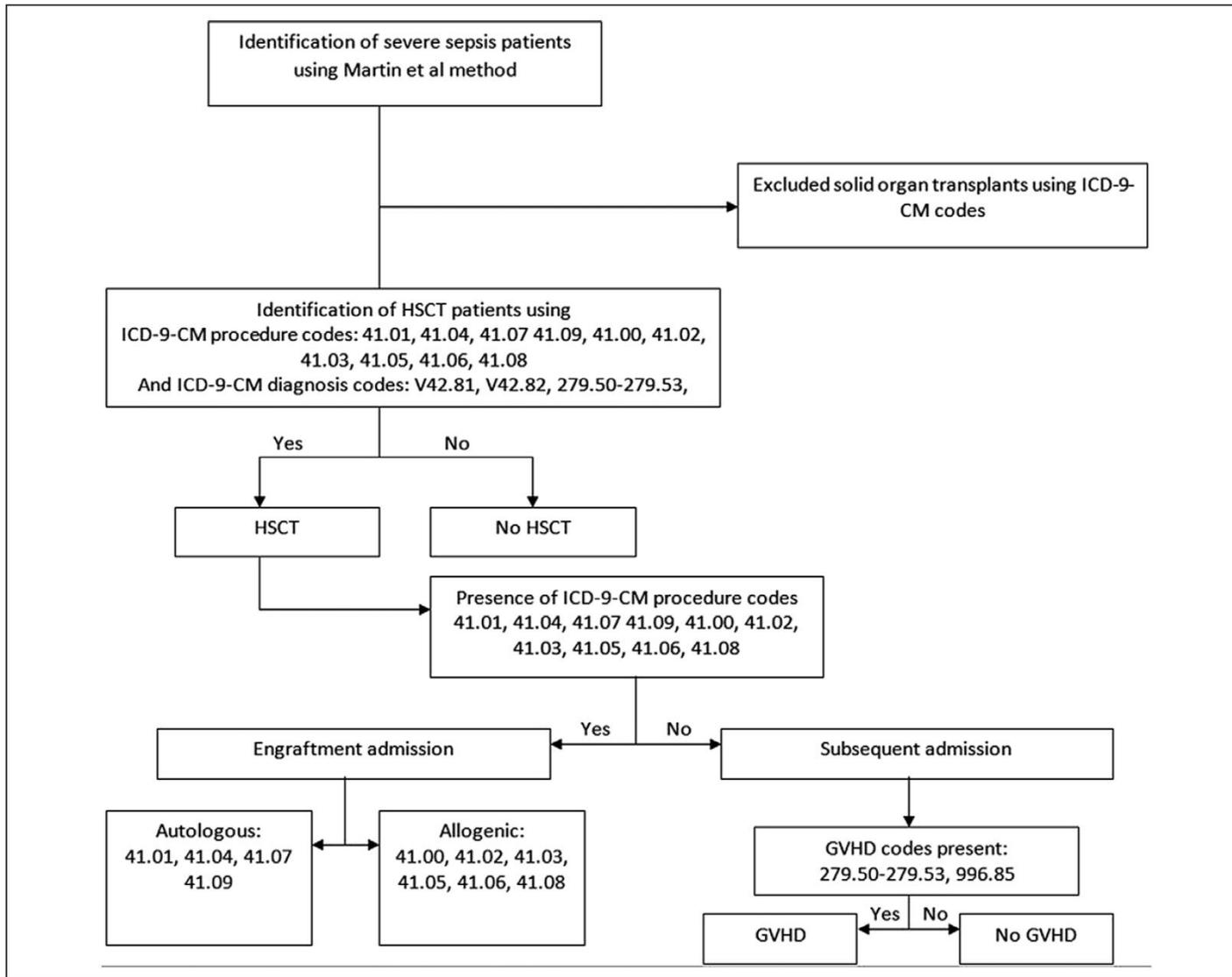


Figure 1. Identification and grouping of hematopoietic stem cell transplant (HSCT) patients into four groups. GVHD = graft-versus-host disease, ICD-9-CM = *International Classification of Diseases*, 9th Edition, Clinical Modification.

TABLE 1. Demographic Characteristics of Hematopoietic Stem Cell Transplant Patients Admitted With Severe Sepsis From 2000 to 2008

Variable	Non-HSCT	HSCT			
		Engraftment Admission		Subsequent Admission	
		Autologous	Allogeneic	GVHD	No GVHD
Total admissions	286,285,073	53,337	25,950	64,878	146,909
Severe sepsis, <i>n</i> (%)	4,654,341 (1.6)	2,750 (5.2)	3,418 (13.2)	6,713 (10.4)	9,017 (6.1)
Age category, ^a yr					
18–34	3.9	10.8	26	22.4	13.5
35–49	10.6	20.4	33.4	32	24.9
50–64	22.9	47.2	36.3	39.3	45.8
≥ 65	62.7	21.6	4.3	6.3	15.7
Sex ^a					
Female	49.7	43.4	36.6	39.4	42.6

TABLE 2. (Continued) Clinical Characteristics of Hematopoietic Stem Cell Transplant Patients Admitted With Severe Sepsis Over 2000–2008

Variable	Non-HSCT	HSCT			
		Engraftment Admission		Subsequent Admission	
		Autologous	Allogeneic	GVHD	No GVHD
Infection (%)					
<i>Clostridium difficile</i> ^a	5.9	12	13.4	9.2	5.8
Gram positive ^a	27.8	33	38.3	36.1	32.9
Gram negative ^a	20.9	16	15.8	25.3	22
Aspergillus ^a	0.21	2.2	5.8	5.8	2.8
Candida ^a	1.5	3.3	5.4	2.7	1.6
Procedures (%)					
Invasive mechanical ventilation ^a	39.4	30.9	40.4	37.6	31.8
Tracheostomy ^a	6.8	3.8	5.8	3.4	2.8
Blood ^a	23.6	39.4	35.8	35	37.5
New dialysis ^a	5.7	11.4	19.3	11	8.2
Total parenteral nutrition ^a	6.0	13.7	21.5	17.7	6.8

HSCT = hematopoietic stem cell transplant, GVHD = graft-versus-host disease.

^a $p < 0.0125$.

All comparisons are with non-hematopoietic stem cell transplant group.

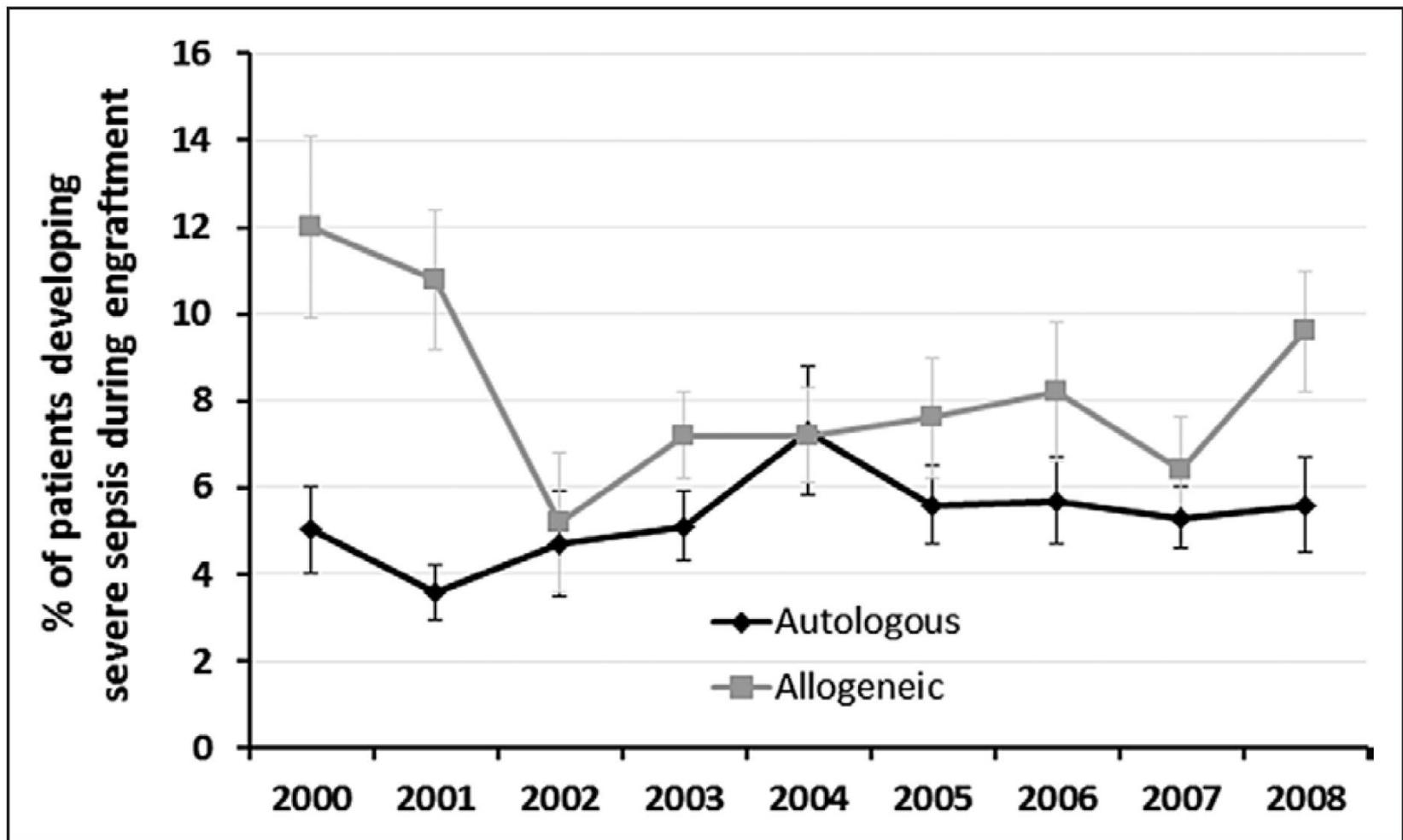


Figure 2. Rate of hematopoietic stem cell transplant recipients developing severe sepsis during engraftment admission.

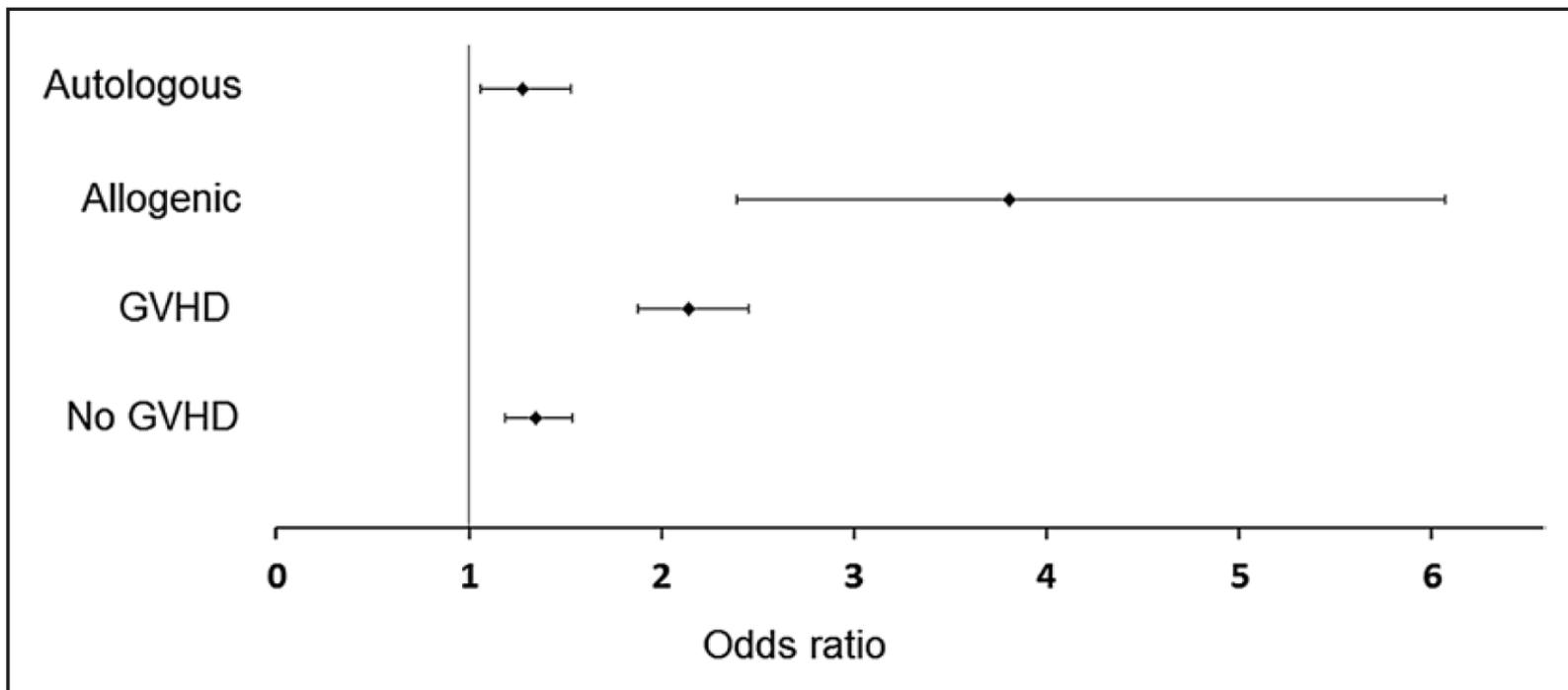


Figure 4. Forrest plot showing odds ratio of mortality in severe sepsis—hematopoietic stem cell transplant admissions compared with nonhematopoietic stem cell transplant. GVHD = graft-versus-host disease.

TABLE 3. Outcomes of Hematopoietic Stem Cell Transplant Patients Admitted With Severe Sepsis Over 2000–2008

Variable	Non-HSCT	HSCT			
		Engraftment Admission		Subsequent Admission	
		Autologous	Allogeneic	GVHD	No GVHD
Mortality (%)	32.9	30.1	55.1 ^a	47.9 ^a	35
Disposition in survivors (%)					
Home	27.3	58.7 ^a	58.4 ^a	45.7 ^a	50.3 ^a
Home care	16	26.9 ^a	33 ^a	33.5 ^a	29 ^a
Facility	49.4	12.7 ^a	6.6 ^a	14.6 ^a	13.2 ^a
Transfers	6.3	1.5 ^a	2.0 ^a	6.1	7.3
Time to death (d) ^b	7 (2–16)	34 (21–54) ^a	44 (27–61) ^a	21 (10–37) ^a	10 (4–23)
Length of stay in survivors (d) ^b	11 (6–20)	26 (21–37) ^a	39 (30–58) ^a	12 (6–29)	9 (5–17)

HSCT = hematopoietic stem cell transplant, GVHD = graft-versus-host disease.

^a $p < 0.0125$.

^bMedian (interquartile range).

All comparisons are made with non-hematopoietic stem cell transplant group.

Syndromes de libération de cytokines et de fuite capillaire

Les toxicités endothéliales

- traitements aux cytokines : IL2, GM-CSF à hautes doses
- certains agents chimiothérapeutiques : docétaxel, gemcitabine
- les immunothérapies (comme le nivolumab)
- greffes de moelle osseuse avec conditionnement
- CAR T cells (chimeric antigen receptor)

Traitements aux cytokines

- Le meilleur exemple est l'interleukine-2
- Tableau clinique: syndrome de fuite capillaire avec rétention hydrique, œdème, gain de poids; hypotension artérielle; insuffisance rénale, oligurie; œdème pulmonaire
- Peut donner des états de choc et un syndrome de défaillance multiviscérale

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Multiple organ failure during interleukin-2 administration and LAK cells infusion

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CAR-T

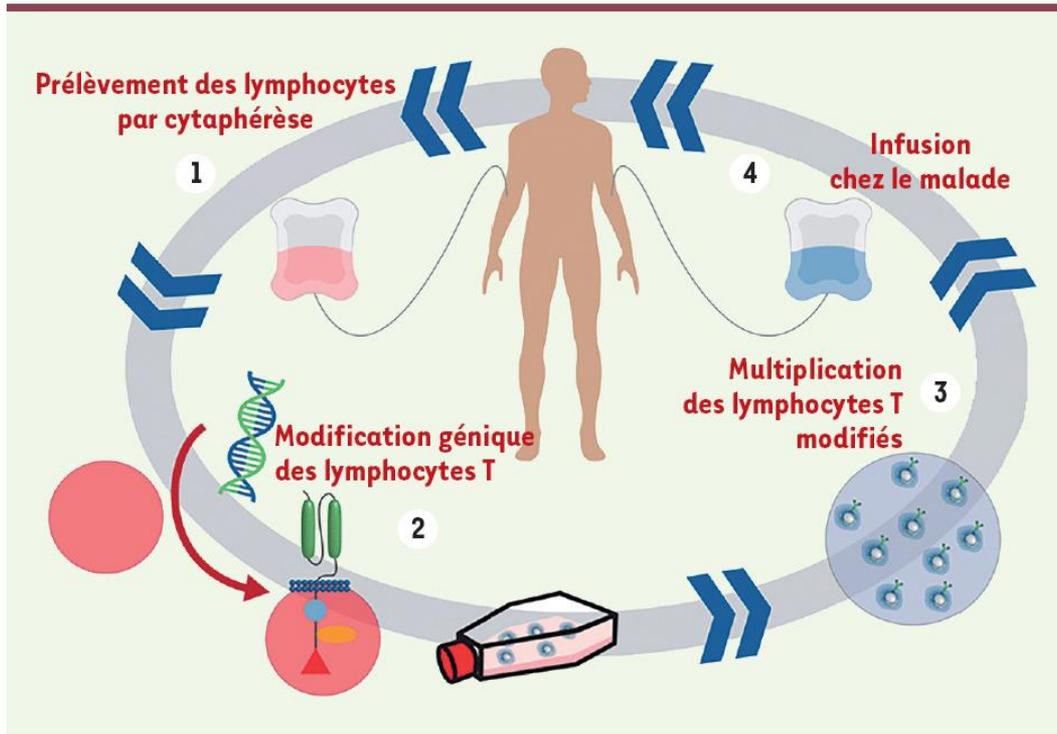


Figure 1. Schéma général d'une thérapie de type CAR-T. Le lymphocyte T modifié (en bas à gauche) exprime un récepteur antigénique chimérique comportant, en surface, deux domaines variables d'immunoglobuline et, à l'intérieur de la cellule, plusieurs domaines d'activation et de stimulation (adapté de *Rockland Immunochemicals*, <https://rockland-inc.com/car-t-cell-therapy-services.aspx>).

Complications

- cytokine release syndrome (CRS): lié à une libération massive de cytokines (fièvre, tachycardie, hypotension, insuffisance rénale, etc.)
- toxicités neurologiques : tremblements, aphasie, convulsions, etc.

Traitement

- arrêt du médicament
- symptomatique : réduire les apports et favoriser la diurèse en maintenant les signes vitaux
- Immunosuppresseurs : tolicilizumab,
corticothérapie : lorsque la vie du patient est en danger

REVIEW

Side-effect management of chimeric antigen receptor (CAR) T-cell therapy

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Chimeric antigen receptor (CAR) T cells directed against the B-cell marker CD19 are currently changing the landscape for treatment of patients with refractory and/or relapsed B-cell malignancies. Due to the nature of CAR T cells as living drugs, they display a unique toxicity profile. As CAR T-cell therapy is extending towards other diseases and being more broadly employed in hematology and oncology, optimal management strategies of side-effects associated with CAR T-cell therapy are of high relevance. Cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and cytopenias constitute challenges in the treatment of patients with CAR T cells. This review summarizes the current understanding of CAR T-cell toxicity and its management.

Key words: Chimeric antigen receptor (CAR) T cells, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), CAR T-cell associated side-effects, CAR T-cell side-effect management

Table 2. Grading and proposed management of cytokine release syndrome (CRS) adapted from ASTCT CRS grading consensus guidelines by Lee et al.⁵¹ and Neelapu⁵³

Grade	Fever	Hypotension ^a	Hypoxia ^a	Management
1	Temperature $\geq 38.0^{\circ}\text{C}$	—	—	Supportive management Antipyretics, IV hydration infectious diagnostic work-up; initiate anti-infective treatment
2		No vasopressor required	Low-flow O ₂ (≤ 6 l/min; nasal canula)	Continue supportive management of CRS grade 1 IV fluid boluses Supplemental oxygen Tocilizumab (8 mg/kg BW/dose in patients ≥ 30 kg BW; 12 mg/kg BW in patients < 30 kg BW; IV administration; maximum of 800 mg/dose) \pm corticosteroids (dexamethasone 10 mg every 6-8 h or methylprednisolone equivalent)
3		1 vasopressor	High-flow O ₂ (≥ 6 l/min; high-flow nasal canula, mask, NIV)	Continue supportive management of CRS grade 1 Consider ICU management Vasopressor support and/or supplemental O ₂ Tocilizumab (8 mg/kg BW/dose in patients ≥ 30 kg BW; 12 mg/kg BW in patients < 30 kg BW; IV administration; maximum of 800 mg/dose) + dexamethasone 10-20 mg IV every 6 h or methylprednisolone equivalent
4		>1 vasopressor	Positive pressure (CPAP, BiPAP, mechanical ventilation)	Continue supportive management of CRS grade 1 ICU management Vasopressor support and/or supplemental O ₂ via positive pressure Tocilizumab (8 mg/kg BW/dose in patients ≥ 30 kg BW; 12 mg/kg BW in patients < 30 kg BW; IV administration; maximum of 800 mg/dose) + methylprednisolone 1000 mg/day

BiPAP, bilevel positive airway pressure; BW, body weight; CPAP, continuous positive airway pressure; CRS, cytokine release syndrome; ICU, intensive care unit; IV, intravenous; NIV, non-invasive ventilation; O₂, oxygen; PAP, positive airway pressure.

Table 4. Grading and proposed management of immune effector cell-associated neurotoxicity syndrome (ICANS): according to and adapted from ASTCT ICANS grading consensus guidelines by Lee et al.⁵¹ and Neelapu⁵³

Grade	ICE score	Consciousness	Seizure	Motor findings	Elevated ICP/edema	Management
1	7-9	Awakens spontaneously	—	—	—	Supportive management EEG Neuroimaging Lumbar puncture Tocilizumab only if concurrent CRS
2	3-6	Awakens to voice	—	—	—	Continue supportive management of ICANS grade 1 Consider dexamethasone 10 mg ever 6-8 h or methylprednisolone equivalent
3	0-2	Awakens only to tactile stimulus	Any seizure that resolves rapidly ± intervention	—	Focal or local edema on imaging	Continue supportive management of ICANS grade 1 ICU treatment recommended Dexamethasone 10-20 mg IV every 6 h or methylprednisolone equivalent Control seizures with anti-epileptics Treat focal/local edema with methylprednisolone 1000 mg/day Consider airway protection
4	0 ^a	Vigorous stimuli required, unarousable, stupor, coma	Prolonged life-threatening seizure (>5 min) or repetitive seizure without return to baseline	Deep focal weakness, i.e. hemiparesis, paraparesis	Diffuse cerebral edema on imaging or papilledema or decerebrate/decorticate posture or cranial nerve VI palsy or Cushing's triad (bradycardia, hypertension and abnormal breathing)	Continue supportive management of ICANS grade 1 ICU treatment High-dose methylprednisolone 1000 mg/day Airway protection, e.g. by intubation and mechanical ventilation Control seizures with anti-epileptics Lower elevated ICP with hyperventilation, hyperosmolar therapy or neurosurgery

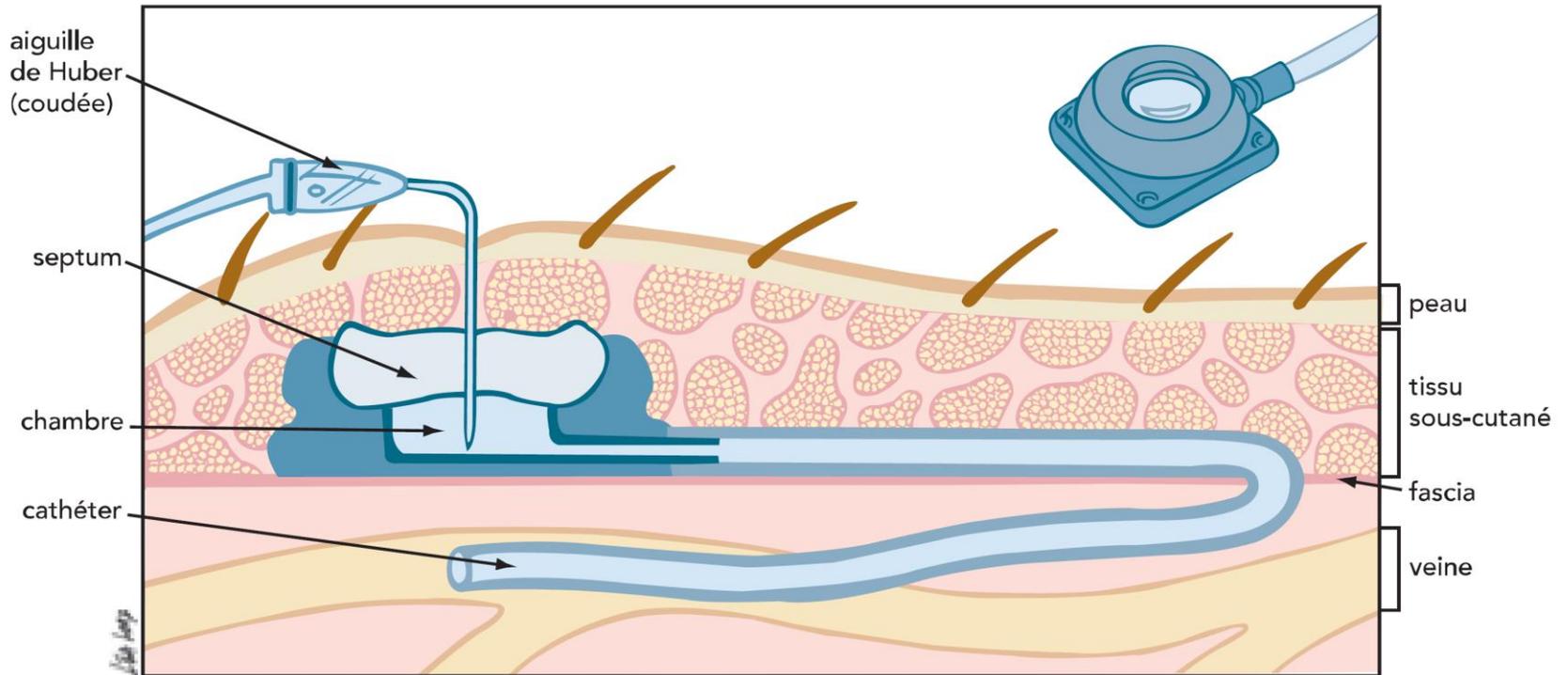
CRS, cytokine release syndrome; EEG, electroencephalography; ICE, immune effector cell-associated encephalopathy; ICP, intracranial pressure; ICU, intensive care unit.

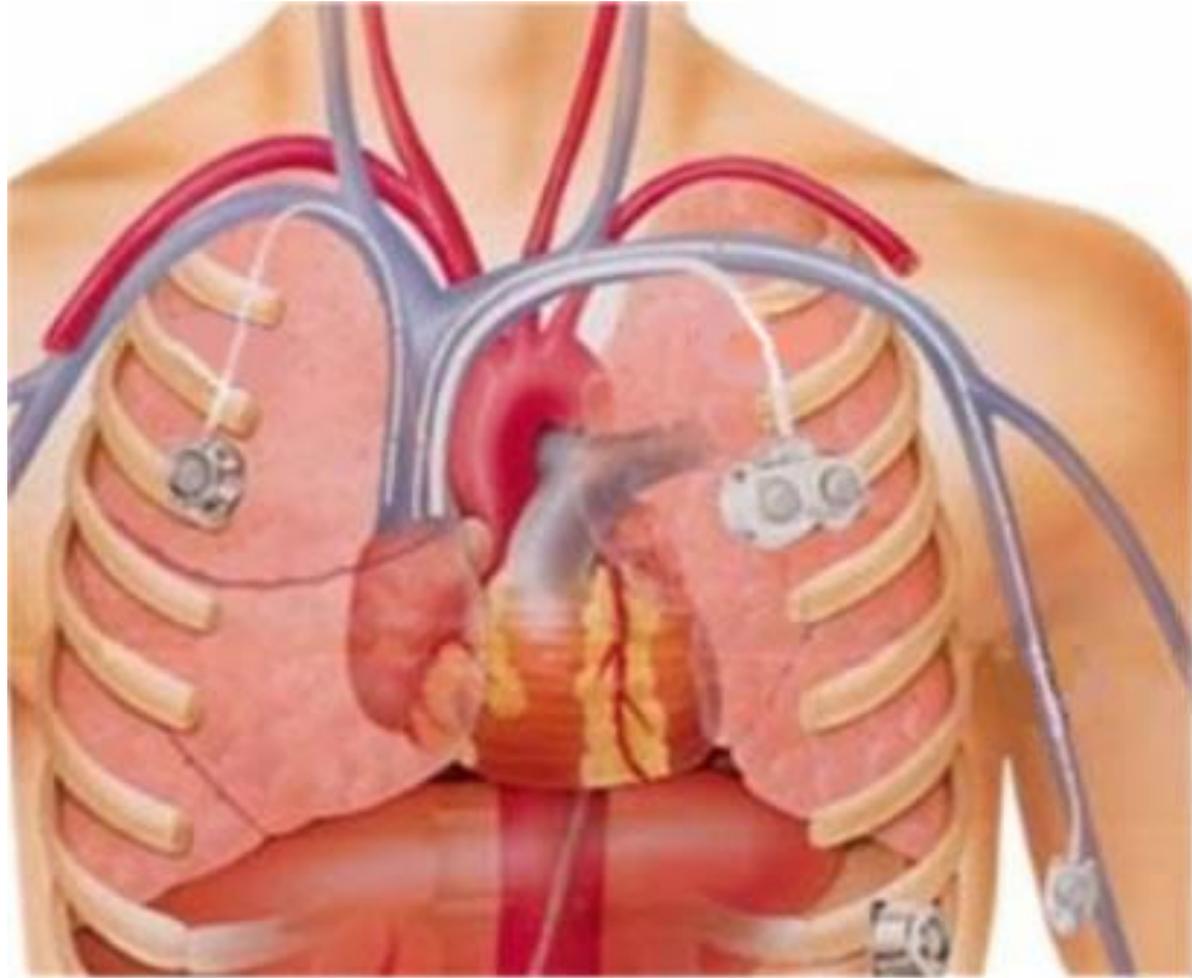
^a ICE score 0 classified as ICANS grade 3 if patient is awake with aphasia; grade 4 if patient is unarousable and unable to perform ICE assessment.

Considérations techniques

Cathéters veineux centraux et cathéters à chambre

Schéma d'une chambre à cathéter implantée en sous-cutané



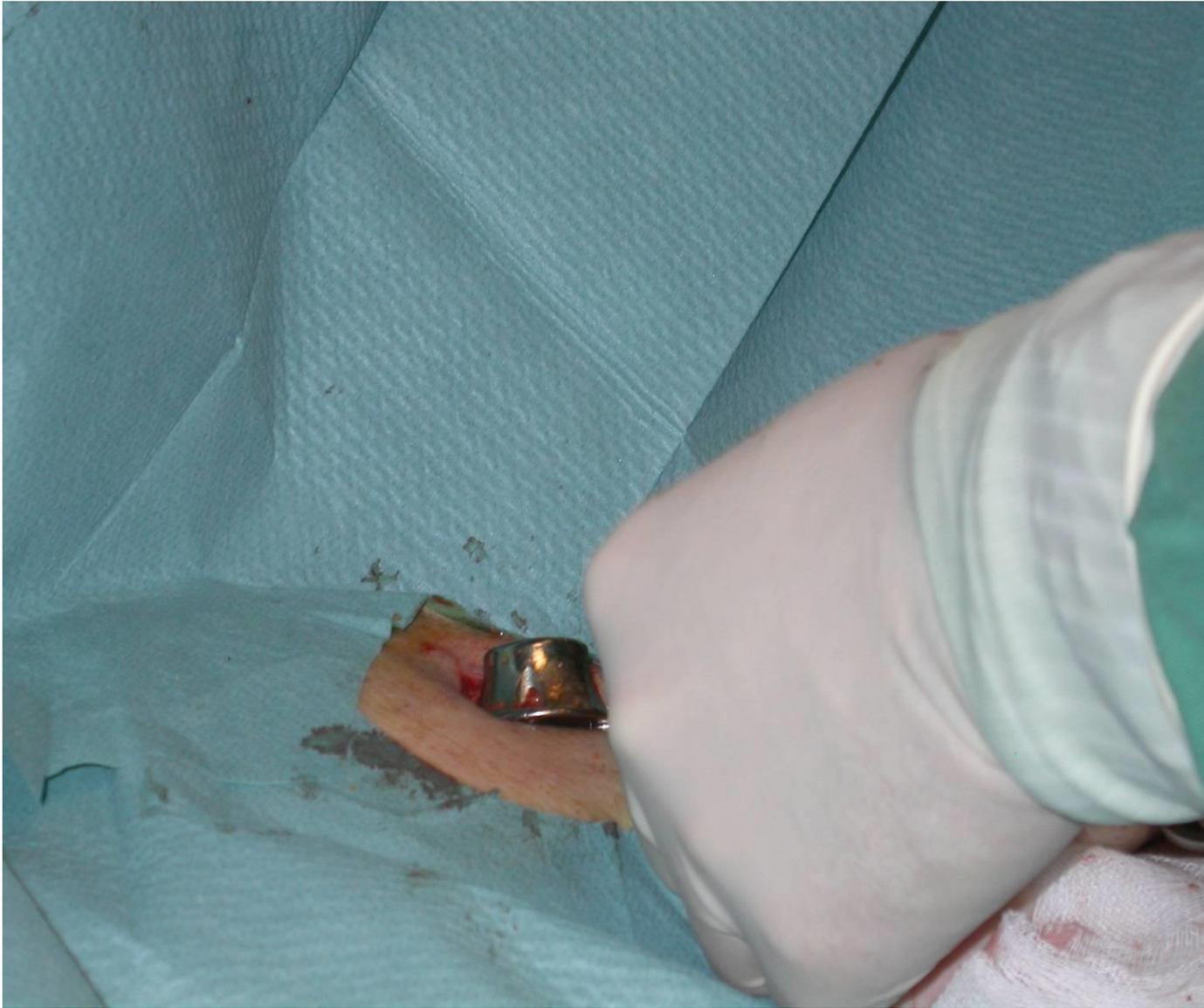


Occlusion du cathéter

- Absence de reflux avec impossibilité d'injection (thrombose et/ou précipités)
- Ne pas essayer de déboucher en forçant (risque de rupture, de migration ou de thrombo-embolie)
- Changer la position du patient, essayer une manoeuvre de Valsalva
- Sinon : déboucher à l'héparine : 5000 U dans 10 ml, essayer d'injecter et retirer l'héparine par bolus de 2 à 5 ml
- En cas d'échec : minifibrinolyse à l'urokinase: 3 heures d'incubation après injection dans le cathéter de 2,5 ml d'une solution à 5.000 UI/ml d'urokinase

Infection cathéter à chambre

- Faire prélèvements adéquats : pus au point d'entrée, hémoculture aspirée par le PAC, hémoculture par voie périphérique
- Tenter un traitement antibiotique par le PAC en couvrant initialement empiriquement les staphylocoques (vancomycine) et en adaptant ensuite aux résultats des hémocultures
- Faire systematiquement des hémocultures de contrôle
- en cas de sepsis sévère ou d'échec : retrait du PAC



Thrombose veineuse cathéter à chambre

- À envisager en cas de douleur et de gonflement dans le territoire d'amont avec éventuellement apparition d'une circulation collatérale
- Faire échographie (et hémocultures pour exclure thrombose septique)
- Traitement par héparine i.v.

Blot; ICM 23 : 1837-1842 ; 2000

**Accuracy of totally implanted ports,
tunnelled, single- and multiple-lumen
central venous catheters for measurement
of central venous pressure**

Cathéters veineux centraux et thrombopénie

Attitude

- En cas de troubles de coagulation, notamment thrombopénies sévères, les cathéters veineux centraux peuvent être placés sans risque majeur sous couverture de transfusions de plaquettes et par un médecin expérimenté.
- Le taux de plaquettes sera maintenu au dessus de $50.000/\text{mm}^3$
- Eventuellement, un guidage par Doppler (échographie) peut s'avérer utile.