ΒΑΡΕΩΣ ΠΑΣΧΩΝ ΚΑΙ ΚΑΚΟΘΗΕΙΑ

Καθηγητής Γιώργος Θ. Δημόπουλος

gdimop@med.uoa.gr

Εθνικό και Καποδιστριακό Πανεπιστήμιο - Ιατρική Σχολή Αθηνών
Β΄Κλινική Εντατικής Θεραπείας, Πανεπιστημιακό Νοσοκομείο ΑΤΤΙΚΟΝ

ΑΤΤΙΚΟΝ

Βαρέως πάσχων και κακοήθεια
Ιστορικό

Δεκαετίες ΄80 και ΄90
- Εντατικολόγος ➔ απέφευγε την εισαγωγή ασθενούς με κακοήθεια στην ΜΕΘ λόγω της κακής έκβασης

2000 και έπειτα
- Έγκαιρη διάγνωση
- Νέες θεραπείες
- Αύξηση εισαγωγών
- Σήψη ➔ δεύτερη αιτία εισαγωγής στη ΜΕΘ (όχι διαφορά από ασθενείς χωρίς κακοήθεια)

Azoulay E et al. Crit Care Med 2001;29:2132-6, Peigne V et al, Intens Care Med 2008;35:512-8,
Azoulay E et l Crit Care Med 2001;29"519-25, Taccone FS et al, Crit Care 2009;13R1S, Soares M et al, Crit Care Med 2010; 389-15

Βαρέως πάσχων και κακοήθεια
Ασθενής με κακοήθεια και σήψη

Ο ασθενής με κακοήθεια είναι πιο επιρρεπής να εμφανίσει σήψη λόγω
- Της ανοσοκαταστολής από τη χημειοθεραπεία
- Της εμφάνισης μεταστάσεων

Ασθενής με ανενεργή κακοήθεια
- Εάν εμφανίσει σήψη ?
- Θεωρείται συνοσηρότητα που θα επηρεάσει την έκβαση ?
- Δεδομένα πολύ περιορισμένα

Williams MO et al Crit Care 2004;8R291-8

Βαρέως πάσχων και κακοήθεια
Ασθενείς με αιματολογικές κακοήθειες στη ΜΕΘ

Η διαλογή (triage) για εισαγωγή στη ΜΕΘ διαφέρει <3-70%

Η έκβαση των ασθενών αυτών διαφέρει επίσης

- Περιορισμένες διαθέσιμες κλίνες ΜΕΘ
  - (6.6/100.000 πληθυσμού στο Ην. Βασίλειο)
- Καθυστερημένη εισαγωγή στη ΜΕΘ
- Επιβίωση 2.5%-60%

Νέα μέθοδος

- Critical Care Outreach Services (CCOS)
- 7day, 24h υπηρεσία που αποτελείται από 2 νοσηλεύτριες και έναν εξειδικευόμενο «παλιό» εντατικολόγο
- Ειδικευμένος εντατικολόγος – διαθέσιμος 5 days/εβδομάδα, 08.00-18.00
- Τις υπόλοιπες ώρες : on call εφημερεύων

Βαρέως πάσχων και κακοήθεια
CCOS (Critical Care Outreach Services)

Απευθείας κλήση από ιατρικό προσωπικό ορόφου
NEWS score (National Early Warning Score)

- Score >4 επανεκτίμηση ασθενούς από προσωπικό ορόφων
- Score >6 συναγερμός CCOS
- Συνοσηρότητες
- Κατάσταση ασθενούς
- Συμβουλές (υγρά, αγγειοσυσπαστικά)
- HFNCO (High Flow Nasal Canula Oxugen) = 60L/min
- Ωριαία εκτίμηση κατάστασης ασθενούς
- Σύσταση για εισαγωγή στη ΜΕΘ
- End of Life

Βαρέως πάσχων και κακοήθεια
CCOS (Critical Care Outreach Services)

Reason for referral*	
NEWS	22 (17.5%)
Hypoxia	34 (27.0%)
Low GCS	6 (4.8%)
Hypotension	15 (11.9%)
Sepsis	31 (24.6%)
Other	18 (14.3%)
Number of reviews per patient	4 (2–6)
Length of review (days) per patient	3 (1–5)
Intervention	
Advice	52 (41.3%)
ICU admission	39 (31.0%)
HFNCO	10 (7.9%)
EoL	25 (19.8%)

Βαρέως πάσχων και κακοήθεια
Αμεση εισαγωγή στη ΜΕΘ

	Univariate analysis			Multivariable analysis[a]		
Variables	**OR**	**95%CI**	***p* value**	**OR**	**95%CI**	***p* value**
Reason for referral						
NEWS	1	1	1	1	1	1
Sepsis	2.125	0.693–6.514	0.187	19.605	2.387–161.008	0.006
Hypoxia	2.217	0.737–6.668	0.157	12.703	1.715–94.092	0.013
Hypotension	1.250	0.334–5.162	0.697	14.247	1.343–151.104	0.027
Other	1.312	0.381–4.104	0.713	6.619	0.684–64.057	0.103
Number of referrals	1.098	1.009–1.196	0.031	1.191	1.031–1.375	0.017

Variables influencing ICU admission

	Univariate analysis			Multivariable analysis[a]		
Variables	**OR**	**95%CI**	***p* value**	**OR**	**95%CI**	***p* value**
Length of review (days)	1.064	0.985–1.149	0.117	1.243	1.048–1.473	0.012
Status						
Remission	1	1	1	1	1	1
Relapse	3.392	1.140–10.093	0.028	4.472	1.266–15.791	0.020
Progression	11.100	2.141–57.535	0.004	12.353	1.876–81.354	0.009
Refractory	4.317	1.100–16.939	0.036	4.287	0.816–22.517	0.085

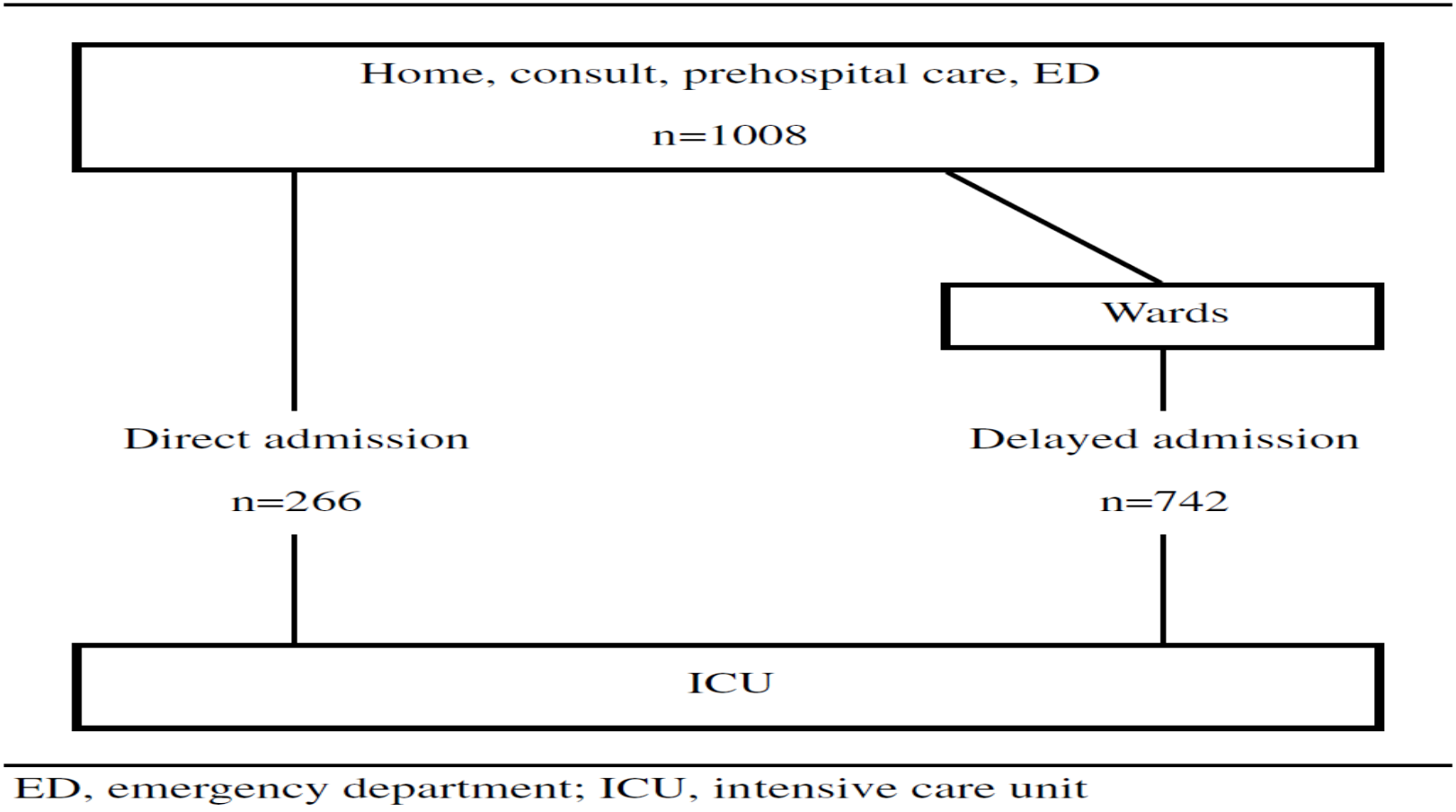
Variables influencing hospital mortality

Taheri L et al J Intens Care Society 2019;20(4)327-34

Βαρέως πάσχων και κακοήθεια
Ασθενείς με αιματολογικές κακοήθειες στη ΜΕΘ

Πιθανότητες εισαγωγής στη ΜΕΘ	
Σημεία ή Συμπτώματα	**Πιθανότητες (αυξημένες)**
Σήψη	20
Υπόταση	14
Υποξία	13
Κακή έκβαση (από εισαγωγή στο Νοσοκομείο)	
Για κάθε ημέρα CCOS	1.27
Επιδείνωση βασικής νόσου	4-12
Μείωση εισαγωγής στη ΜΕΘ	
HFNCO	Ανεξάρτητα από νόσο ή κατάσταση ασθενούς

Βαρέως πάσχων και κακοήθεια
Αμεση εισαγωγή στη ΜΕΘ



ED, emergency department; ICU, intensive care unit

Peyrony O et al Ann Intens Care 2019

Βαρέως πάσχων και κακοήθεια
Αμεση εισαγωγή στη ΜΕΘ

Variables	Model without imputation ($N = 898$)			Model with imputation ($N = 1008$)		
	OR	95% CI	*P*	OR	95% CI	*P*
Direct admission to the ICU from the ED	0.64	(0.45 to 0.92)	0.02	0.63	(0.45 to 0.88)	0.007
Age > 60 years	1.47	(1.04 to 2.10)	0.03	1.47	(1.05 to 2.04)	0.02
Disease status						
Remission or newly diagnosed	1.00					
Other	1.49	(1.08 to 2.06)	0.01	1.52	(1.12 to 2.07)	0.008
Allogeneic BMT/HSCT recipient	2.46	(1.57 to 3.86)	< 0.0001	2.42	(1.58 to 3.71)	< 0.0001
Charlson (/point)	1.06	(0.99 to 1.14)	0.10	1.07	(1.00 to 1.15)	0.04
Poor PS (> 2)	1.88	(1.30 to 2.72)	< 0.001	1.99	(1.40 to 2.83)	0.0001
SOFA score (/point)	1.24	(1.19 to 1.29)	< 0.00001	1.23	(1.19 to 1.28)	< 0.00001
Reason for ICU admission						
Sepsis or septic shock	1.00					
Acute respiratory failure	2.16	(1.47 to 3.2)	< 0.001	2.11	(1.45 to 3.06)	< 0.0001
Coma	1.68	(0.89 to 3.15)	0.10	1.72	(0.94 to 3.15)	0.08
Metabolic disorder or acute kidney injury	2.05	(1.17 to 3.56)	0.01	2.12	(1.24 to 3.62)	0.006
Other	2.17	(1.30 to 3.63)	0.003	2.25	(1.38 to 3.67)	0.001

BMT bone marrow transplantation, *ED* emergency department, *HSCT* hematopoietic stem-cell transplantation, *ICU* intensive care unit, *PS* performance status, *SOFA* Sequential-Related Organ Failure Assessment

Past history of stage I/II solid tumor malignancy impacts considerably on sepsis mortality: a propensity score matching analysis from the hellenic sepsis study group

George Dimopoulos[1], Nikoletta Rovina[2], Maria Patrani[3], Eleni Antoniadou[4], Dimitrios Konstantonis[1], Konstantina Vryza[5], Glykeria Vlachogianni[6], Miltiades Kyprianou[7], Christina Routsi[8], Evangelos J. Giamarellos-Bourboulis[7,9*] and on behalf of the Hellenic Sepsis Study Group

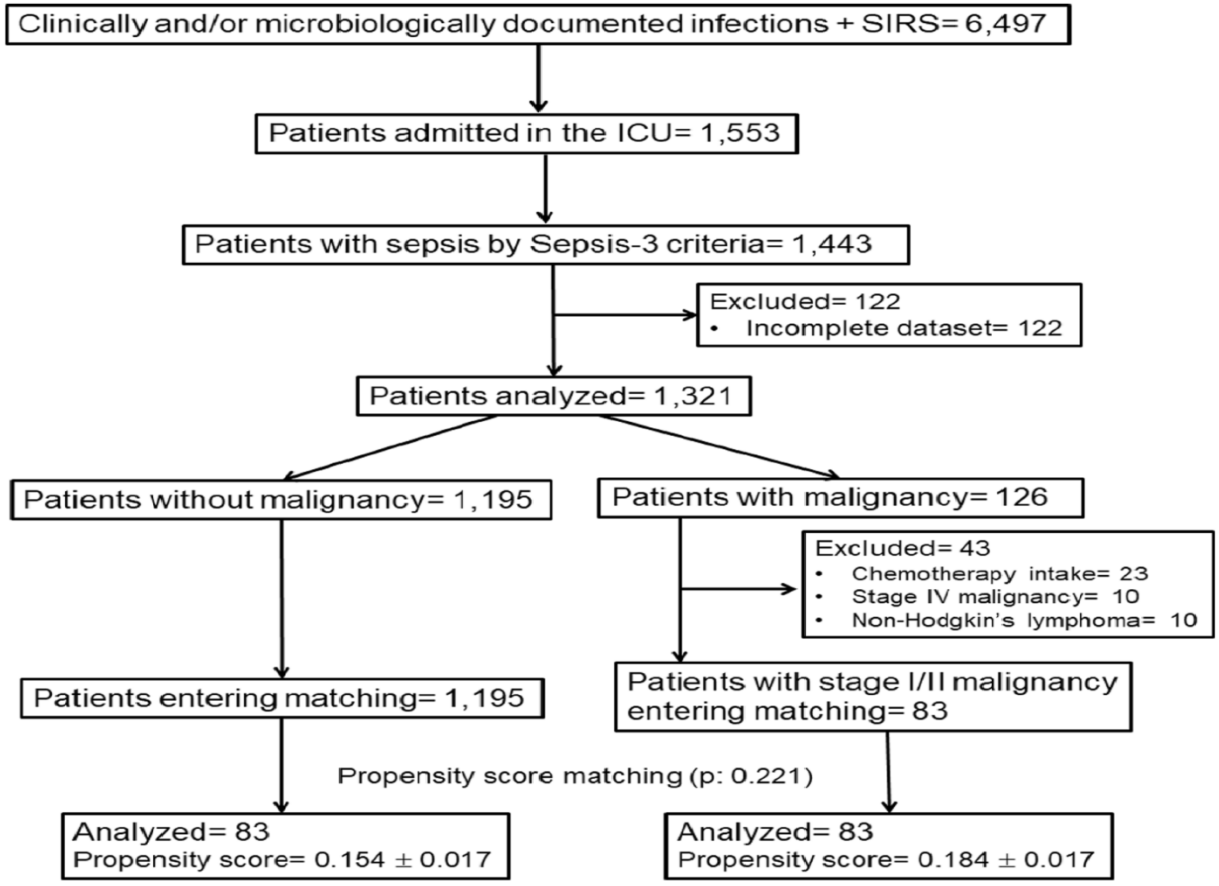


Fig. 1 Study flow chart. Abbreviations ICU: intensive care unit; SIRS: systemic inflammatory response syndrome

Past history of stage I/II solid tumor malignancy impacts considerably on sepsis mortality: a propensity score matching analysis from the hellenic sepsis study group

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Variable	Hazard ratio	95% confidence intervals	*p*-value
Septic shock	1.80	1.01–3.22	0.046
Acute kidney injury	2.06	1.21–3.49	0.007
History of coronary heart disease	0.36	0.14–0.89	0.028
History of stage I/II solid malignancy	1.79	1.13–2.85	0.014

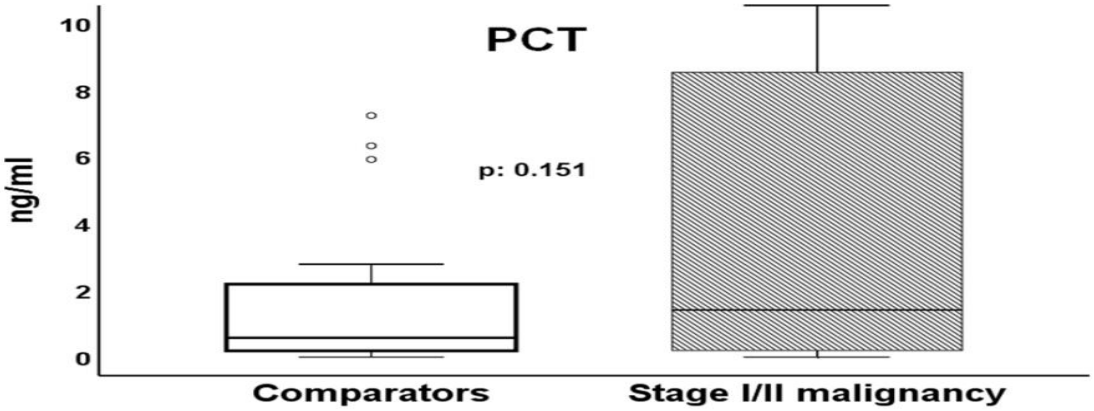
Forward step-wise Cox regression analysis of variables associated with 28 days mortality

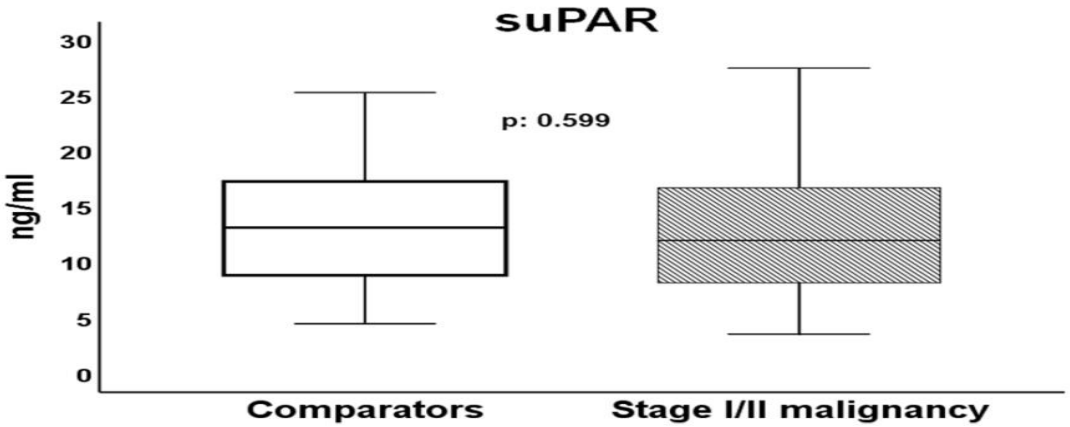
Variable	Hazard ratio	95% confidence intervals	*p*-value
Septic shock	1.45	0.67–3.15	0.345
Acute kidney injury	2.06	0.94–4.55	0.073
History of coronary heart disease	0.74	0.25–2.19	0.587
Susceptibility of the pathogen to the administered antimicrobials	0.54	0.26–1.11	0.096
History of stage I/II solid malignancy	2.72	1.37–5.40	0.004

Cox regression analysis of variables associated with 28 days mortality among patients with microbiologiacally confrimed infections

BMC Infect Dis 2019

Βαρέως πάσχων και κακοήθεια
Συγκεντρώσεις PCT και suPAR

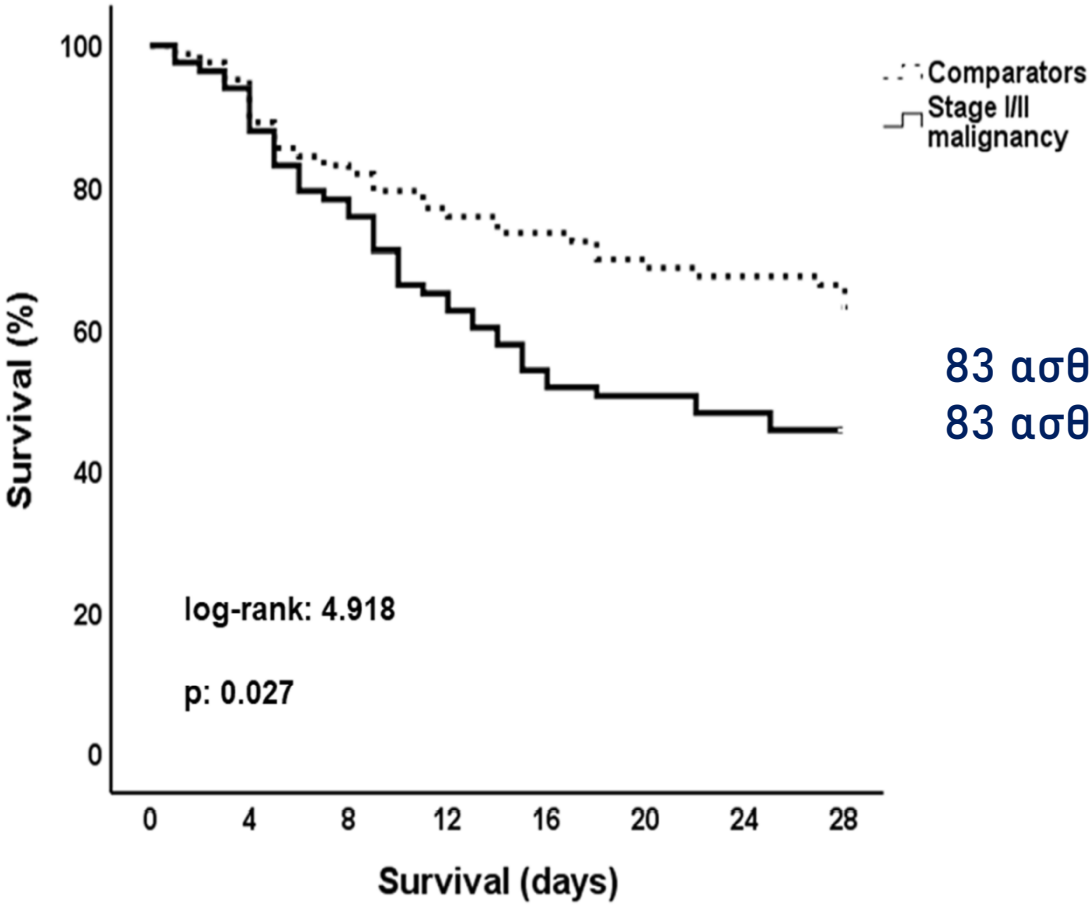




BMC Infect Dis 2019

Βαρέως πάσχων και κακοήθεια

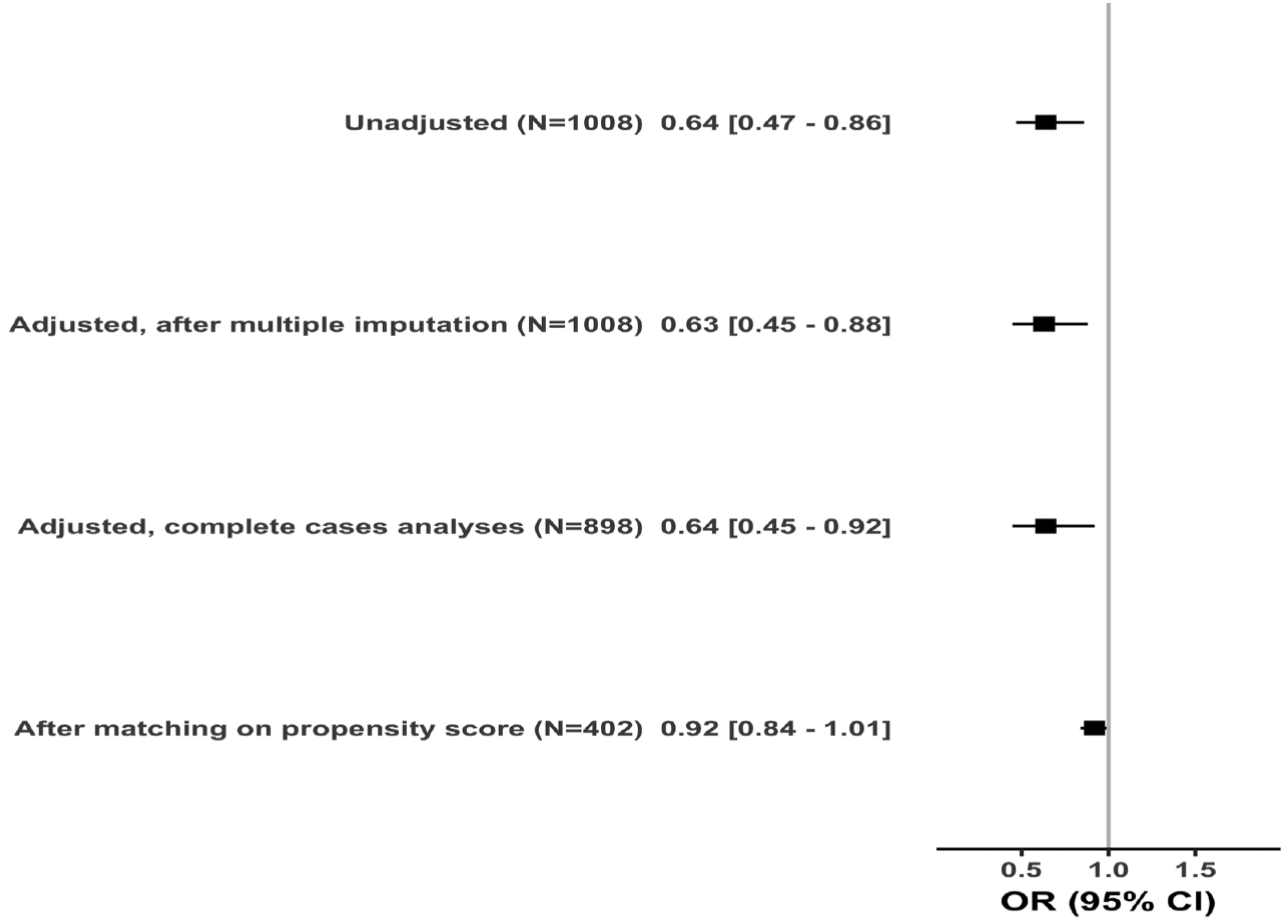
Εκβαση ασθενών με κακοήθεια και σήψη



83 ασθενείς με κακοήθεια και σήψη
83 ασθενείς με σήψη, χωρίς κακοήθεια

BMC Infect Dis 2019

Βαρέως πάσχων και κακοήθεια
Αμεση εισαγωγή στη ΜΕΘ



Peyrony O et al Ann Intens Care 2019

Βαρέως πάσχων και κακοήθεια

Ασθενείς με κακοήθεια συμπαγών οργάνων στη ΜΕΘ

Characteristic	Total	Oncologic Patients	Nononcologic Patients	*P* (oncologic v nononcologic patients)
No. of Patients	301	100	201	
Demographic				
Male, % (No.)	57 (170)	51 (51)	59 (119)	.110
Mean age, years (SD)	59 (19)	64 (15)	57 (21)	.001
Mean ICU acuity assessment (SD)				
APACHE II score	15 (8)	15 (8)	16 (9)	.419
SOFA day 1 score	7 (3)	6 (3)	7 (3)	.083
SOFA day 3 score	5 (4)	5 (4)	5 (4)	.893
SOFA day 5 score	5 (4)	5 (4)	5 (4)	.728
P/F ratio	263 (205)	249 (109)	269 (232)	.525
Lactate, mg/dL	32 (40)	29 (28)	33 (44)	.481
Comorbidities, % (No.)				
Arterial hypertension	35 (108)	32 (32)	37 (75)	.372
Diabetes mellitus	20 (60)	21 (21)	19 (39)	.760
COPD	15 (45)	14 (14)	15 (31)	.864
Chronic kidney disease	6 (18)	4 (4)	8 (16)	.792
Cirrhosis	7 (21)	6 (6)	7 (15)	.796
Other	13 (39)	11 (11)	14 (28)	.586
Mean Charlson comorbidity index (SD)	4 (3)	7 (3)	3 (2)	< .001
Admission syndromes, % (No.)				
Acute respiratory failure	47 (141)	53 (53)	47 (94)	.533
Circulatory shock	41 (122)	39 (39)	42 (83)	.400
Surgical	46 (139)	44 (44)	47 (95)	.625

Lopez R et al. J Global Oncol 2019

Βαρέως πάσχων και κακοήθεια

Ασθενείς με κακοήθεια συμπαγών οργάνων στη ΜΕΘ

Characteristic	No. of Oncologic Patients (%; n = 100)	Mortality, No. of Patients (%)		
		In ICU	At 28 Days	At End of Follow-Up
Cancer type				
Hematologic	10 (10)	4 (40)	5 (50)	8 (80)
Lung	11 (11)	3 (27)	3 (27)	4 (36)
Breast	6 (6)	0 (0)	0 (0)	3 (50)
Colon	8 (8)	0 (0)	0 (0)	1 (13)
Gastric	2 (2)	0 (0)	0 (0)	2 (100)
Other	63 (63)	5 (8)	11 (18)	25 (40)
Solid tumor stage				
All stages	90 (90)	10 (11)	14 (16)	36 (40)
I	4 (4)	0 (0)	0 (0)	0 (0)
II	31 (31)	1 (3)	2 (7)	5 (16)
III	14 (14)	0 (0)	1 (7)	4 (29)
IV	51 (51)	9 (18)	11 (22)	27 (53)
ECOG PS				
0	3 (3)	1 (33)	1 (33)	1 (33)
1	70 (70)	7 (10)	9 (13)	27 (39)
2	22 (22)	4 (18)	8 (36)	13 (59)
3	5 (5)	3 (60)	3 (60)	4 (80)
4	0 (0)	NA	NA	NA
ICU criterion of admission				
Full code	76 (76)	10 (13)	15 (20)	30 (40)
ICU trial	24 (24)	6 (25)	8 (33)	17 (71)
ICU admission reason				
Febrile neutropenia or neutropenic infections	10 (10)	3 (30)	4 (40)	6 (60)
Other postchemotherapy admission	7 (7)	1 (14)	2 (29)	6 (86)
Postoperative admission	44 (44)	2 (5)	3 (7)	12 (27)
Other ICU admission	39 (39)	10 (26)	14 (36)	23 (59)

Lopez R et al. J Global Oncol 2019

Βαρέως πάσχων και κακοήθεια

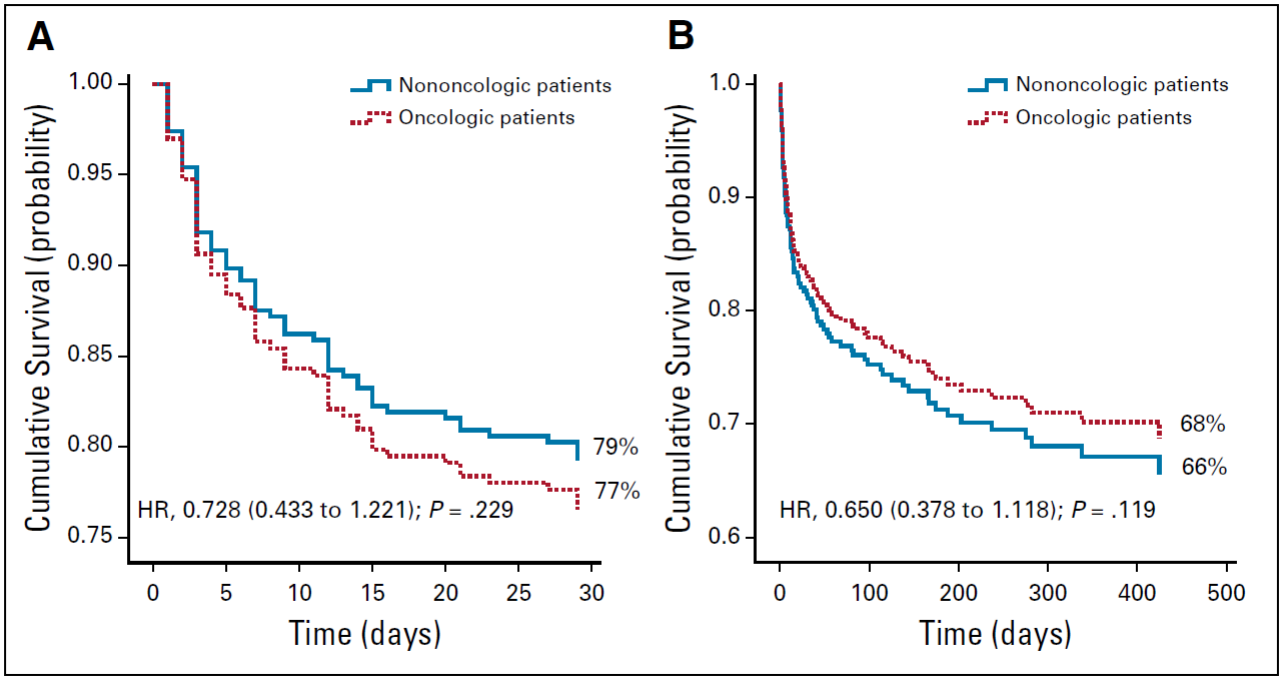
Ασθενείς με κακοήθεια συμπαγών οργάνων στη ΜΕΘ

Outcome	All Patients	Oncologic Patients	Nononcologic Patients	*P* (oncologic *v* nononcologic patients)
Mean length of IMV, days (SD)	4 (5)	5 (5)	4 (4)	.260
Mean ICU LOS, days (SD)	8 (10)	6 (8)	9 (11)	.009
ICU mortality, %	15	16	14	.375
Mortality at 28 days, %	22	23	21	.345
Mortality at end of follow-up, %	31	48	24	< .001
Median long-term follow-up, days (IQR)	148 (42-363)	135 (36-277)	171 (47-406)	.004

Lopez R et al. J Global Oncol 2019

Βαρέως πάσχων και κακοήθεια

Ασθενείς με κακοήθεια συμπαγών οργάνων στη ΜΕΘ



COVID-19 and immunosuppression

Prior Immunosuppressive Therapy and SARS-CoV-2 Severe Illness

- 39,686 adults with a positive PCR test
- **Primary analysis**
  - prior prednisone use ***was associated*** with severe illness after diagnosis (OR 1.31; 95% CI 1.08–1.60
  - Immunomodulator (OR 0.88; 95% CI 0.57–1.34) and biologic/small-molecule therapy (OR1.26;95% CI 0.79–2.00) ***were not associated***
- **Secondary analyses showed variable risk among therapies**
  - Janus-kinase inhibitors : ***increased odds*** of severe illness (OR 3.35; 95% CI 1.16–9.67),
  - thiopurines/conventional disease-modifying antirheumatic drugs : ***reduced odds*** (OR 0.53; 95% CI 0.32–0.88)
  - Tumor necrosis factor inhibitors ***were not associated*** (OR 0.45; 95% CI 0.18–1.08).

Velayos et al.: J Gen Intern Med 2021 DOI: 10.1007/s11606-021-07152-2

COVID-19 : kidney transplantation

Table 1 | Clinical characteristics and outcome of 7 kidney transplant patients with COVID-19 infection

Patient	Age/sex	Tx date	Comorbidities	Respiratory and renal involvement	Baseline creatinine (eGFR ml/min per 1.73 m^2)	Baseline immunosuppression and treatment	ACEI or ARB	Outcome
1	48/M	1989	HT	No	350 (15–18)	Aza/Pred No change	No	Stayed at home, full recovery
2	67/F	03/2019	T2D/HT	Yes, ARDS + AKI (CVVH)	150 (45)	Tac/MMF/Pred MMF stopped	Yes ACEI	Died
3	54/F	12/2019	PTDM/CMV	Yes, ARDS + AKI (CVVH)	132 (48)	Tac/MMF/Pred Tac and MMF stopped	No	Alive, ventilated
4	65/M	08/2018	Wheelchair/ HTN	No ARDS	180 (23)	Tac/MMF/Pred MMF stopped	No	Alive, in medical ward
5	69/F	02/2020	DM/HT	No ARDS AKI	165 (31)	Tac/MMF/Pred MMF stopped	No	Brief ITU stay, not intubated; stepped down to ward
6	54/M	05/2013	Hemolytic anemia/HT	No ARDS	187 (47)	Tac/MMF MMF stopped	No	Stayed at home, still has cough and some flu-like symptoms
7	45/M	09/2017 (2nd Tx)	HT	No ARDS AKI (HD)	450 (12–16)	Tac/Aza/Aza Aza stopped Tac dose reduced	No	Admitted, managed in the ward; severe AKI

Patient	White cell count (× 10^9/l) (3.5–10)	Lymphocyte count (× 10^9/l) (1–3.5)	Serum CRP (mg/l) (<5)	Serum ferritin (µg/l) (25–200)	Serum D dimer (µg/l) (0–500)	Serum LDH (U/l) (100–240)	Serum troponin I (ng/l) (<34)
1	—	—	—	—	—	—	—
2	6 (D1)	0.8 (D1)	83 (D1)		2032 (D3), >6000 (D10)	1226 (D10)	78 (D1), 395 (D10
3	11.25 (D1)	0.5 (D1)	329 (D1)	—	—	—	—
4	—	—	—	—	—	—	—
5	9.4 (D1)	0.3 (D1)	—	—	—	—	30 (D4)[a]
6	10 (D1)	4.0 (D1)	—	—	—	—	—
7	5.5 (D1)	0.3 (D1)	198 (D1)	6919 (D3)	1907 (D3)	502 (D3)	35 (D7)

Banerjee D et al, Kidney International 2020;97:1076-82

COVID-19 and CAR-T cells treatment

Survey by EHA (Scientific Working Group Infection in Hematology)

- 18 European centers - 459 patients treated with CAR-T cells
- Prevalence of COVID-19 : **4.8%**
- Median time from CAR-T therapy and COVID-19 diagnosis : **169 d**
- Severe infection **: 66.7%**
- ICU admission : **43.3%**
- COVID-19 mortality : **33%**
- The disease status at the time of COVID-19 **trended marginally towards adverse outcome** (*P*=0.075)
- In conclusion : a high fatality rate for CAR-T patients with COVID-19, supporting the need to design successful interventions to mitigate the risk of infection in this vulnerable group of patients.

Blood Adv. 2021 Nov 8:bloodadvances.2021005616. doi: 10.1182/bloodadvances.2021005616.

EPICOVIDEHA study

Survey by EHA (Scientific Working Group Infection in Hematology)

- **3801 cases**
  - Lymphoproliferative malignancies
    - ✓ NH lymphoma (1084), Myeloma (684), Chronic Lymphoid Leukemia (474)
  - Myeloproliferative malignancies
    - ✓ Acute myeloid leukemia (497), Myelodysplastic Syndromes (279)
- Severe/critical COVID-19 : **2425 (63.8%)**
- Hospital admission : **2778 (73.1%)**
- ICU admission : **689 (18.1%)**
- Mortality : **1185 patients (31.2%)**

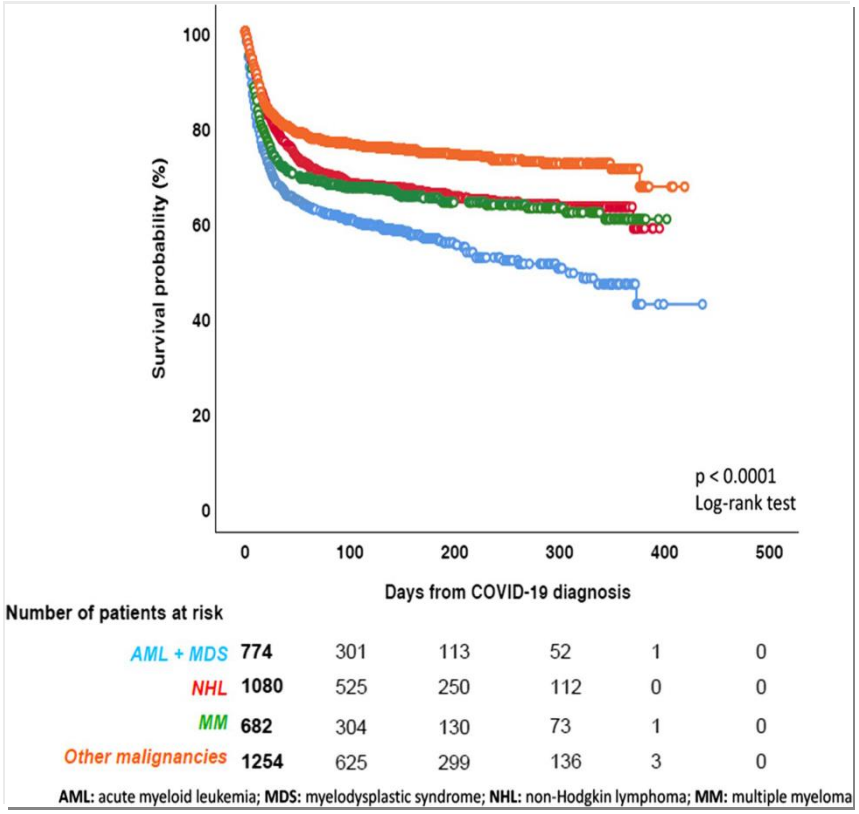
EPICOVIDEHA study

Survey by EHA (Scientific Working Group Infection in Hematology)

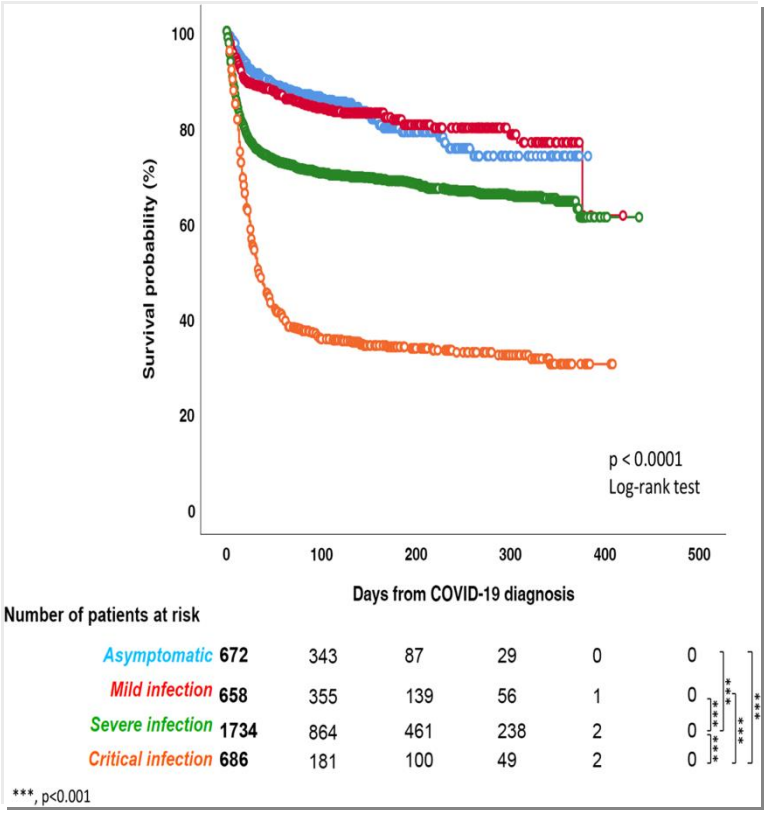
- **Primary cause of death**
  - COVID- 19 : 688 patients **(58.1%)**
  - HM : 173 patients **(14.6%)**
  - Combination of both COVID-19 and progressing HM : 155 patients **(13.1%)**
- **Highest mortality**
  - Acute myeloid leukemia (199/497, 40%)
  - Myelodysplastic syndromes (118/279, 42.3%)
- **Mortality rate significantly decreased between**
  - the first COVID-19 wave (March–May 2020) and the second wave (October–December 2020) (581/1427, 40.7% vs. 439/1773, 24.8%, *p* value < 0.0001)
- **Risk factors correlated with mortality**
  - Age, active malignancy, chronic cardiac disease, liver disease, renal impairment, smoking history, and ICU stay.

Pagano et al. J Hematol Oncol (2021) 14:168

EPICOVIDEHA study



Overall survival by the underlying disease



Overall survival by COVID-19 severity

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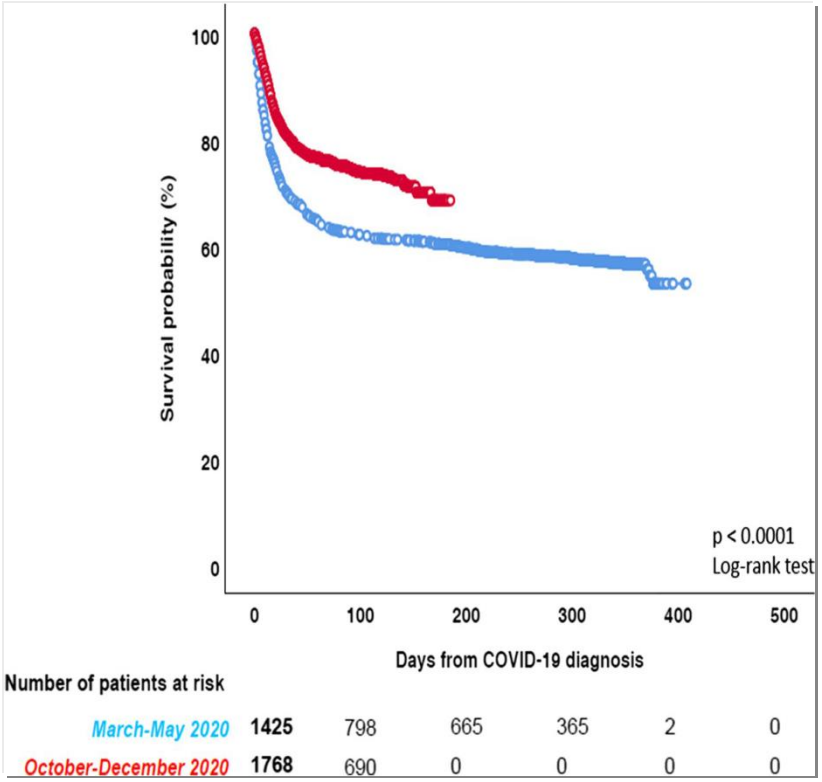
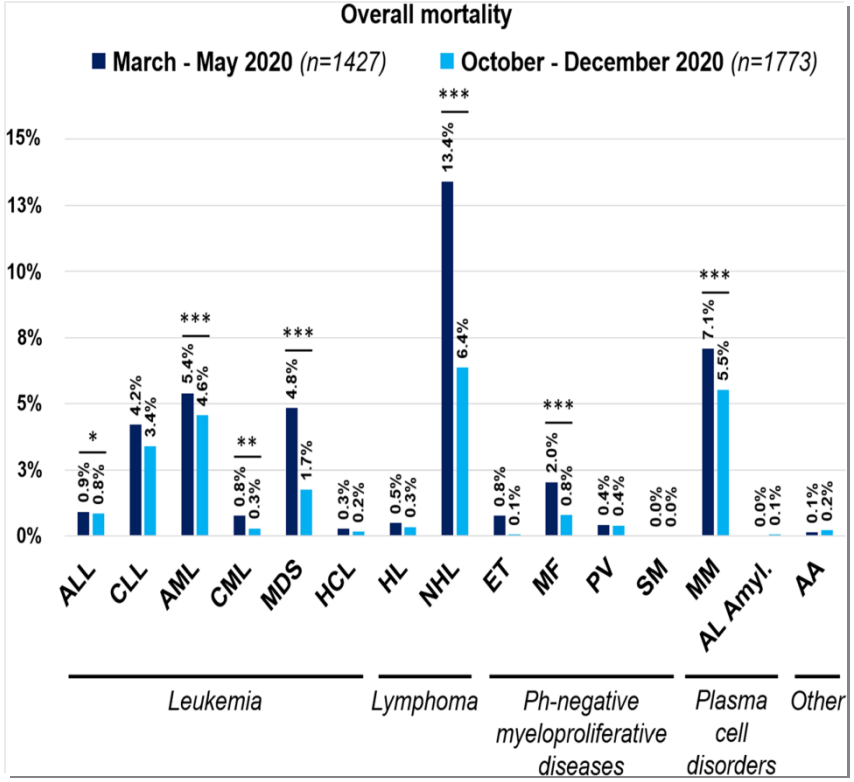
EPICOVIDEHA study



Overall survival by time distribution (first vs. the second wave)



Overall survival in the different HMS by time distribution (first vs. the second wave)

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Immunosuppression and COVID-19

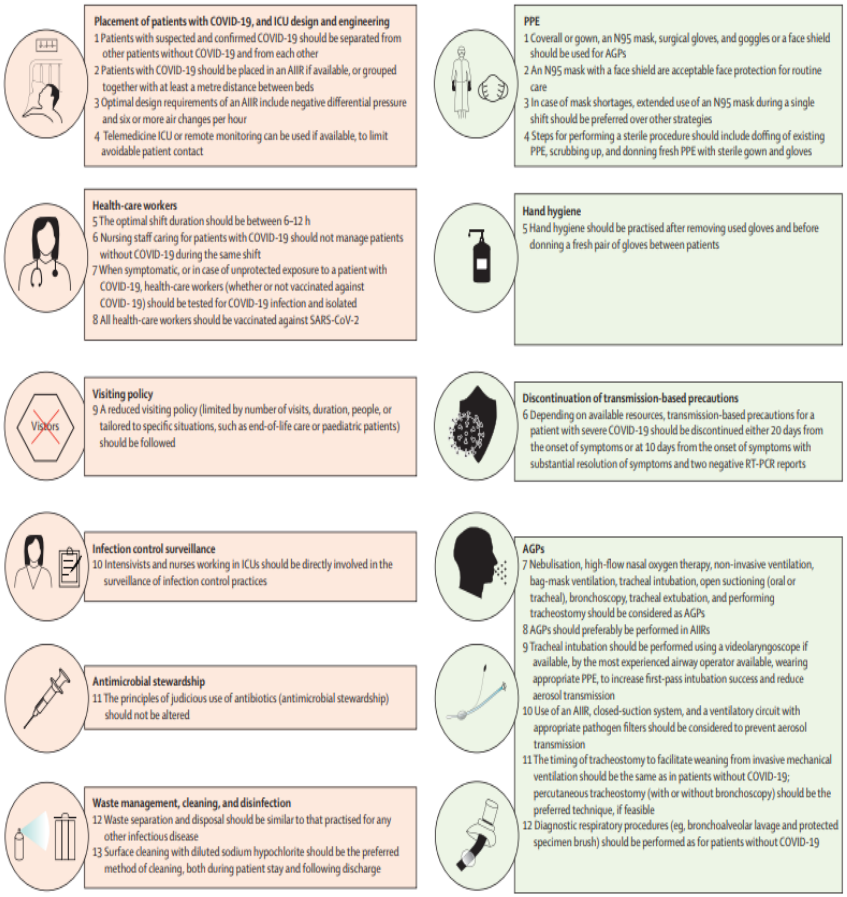
- Retrospective study - University of Chicago Hospitals
- 401 patients with SARS-CoV-2 infection
- Severe COVID-19 illness : 168 (40%)
  - **56 (45%) : past or current cancer**
    - ✓ 25 : severe illness (p=0.76)
  - **55 (44%) : other immunocompromised conditions**
    - ✓ 24 : severe illness (p=0.89)
- Mortality - 30 days post discharge : **13%**
- **Neither cancer (p=0.73) nor immunocompromised conditions (p=0.64) were associated with severe illness.**

Cancer, transplant and immunocompromised are not associated with severe illness or death in hospitalized COVID-19 patients in the ICU.

Krasnow MR et al Journal of Clinical Virology 140 (2021) 104850

Infection control in the intensive care unit: expert consensus statements for SARS-CoV-2 using a Delphi method

Prashant Nasa, Elie Azoulay, Arunaloke Chakrabarti, Jigeeshu V Divatia, Ravi Jain, Camilla Rodrigues, Victor D Rosenthal, Waleed Alhazzani, Yaseen M Arabi, Jan Bakker, Matteo Bassetti, Jan De Waele, George Dimopoulos, Bin Du, Sharon Einav, Laura Evans, Simon Finfer, Claude Guérin, Naomi E Hammond, Samir Jaber, Ruth M Kleinpell, Younsuck Koh, Marin Kollef, Mitchell M Levy, Flavia R Machado, Jordi Mancebo, Ignacio Martin-Loeches, Mervyn Mer, Michael S Niederman, Paolo Pelosi, Anders Perner, John V Peter, Jason Phua, Lise Piquilloud, Mathias W Pletz, Andrew Rhodes, Marcus J Schultz, Mervyn Singer, Jéan-François Timsit, Balasubramanian Venkatesh, Jean-Louis Vincent, Tobias Welte, Sheila N Myatra



***Panel*: Research priorities for infection control of SARS-CoV-2 in ICUs**

ICU design and patient placement
- Optimal design modifications of existing ICUs to control transmission
- Efficacy and safety of remote monitoring to limit cross transmission
- Optimal patient placement strategy

Health-care worker
- Optimal management of a vaccinated health-care worker following unprotected exposure
- Return-to-work criteria for a health-care worker who has recovered from COVID-19

Aerosol generating procedures
- Risk of aerosols generation with individual procedures
- Impact of various strategies in reducing aerosols generation

PPE
- Optimal PPE required for patient management
- Optimal methods to extend use or reuse of PPE

Transmission-based precautions
- Optimal testing strategy for triage of patients with infection
- Optimal transmission-based precautions for variants of SARS-CoV-2
- Effectiveness of movement restriction strategies to prevent cross transmission
- Optimal strategy for discontinuation of transmission-based precautions

Visitor policy
- Optimal strategy for patient visitation

Disinfection and sterilisation
- Role of alternative agents (eg, ultraviolet devices or hydrogen peroxide systems) for terminal room decontamination

Variants of SARS-CoV-2
- Optimal strategies to prevent transmission

Resource-limited settings and during a surge
- Optimal strategies to prevent transmission

Staff transmission
- Optimal strategies to prevent transmission

ICU=intensive care unit. PPE=personal protective equipment.

Lancet Infect Dis. 2021 Nov 10:S1473-3099(21)00626-5.