

How hematologists perceive critical care- Acute myeloid leukemia

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How hematologists perceive critical care...

None out of 398 haematologic patients with multi-organ failure does survive the ICU.

Rubinfeld, Ann Intern Med 1996

Dramatic improvement of ICU survival due to improved patient selection and therapies

→ „Do everything that can be done“

Azoulay, Intensive Care Med 2006

Lecuyer, Crit Care Med 2007

Acute myeloid leukemia and critical care...

The historical perspective:

32 intubated pts. (29 w/ infiltrates):

ICU mortality 97%

Tremblay, Clin Invest Med 1995

30 intubated pts. w/ pulmonary infiltrates: ICU mortality 87%

Rabe, J Crit Care 2004

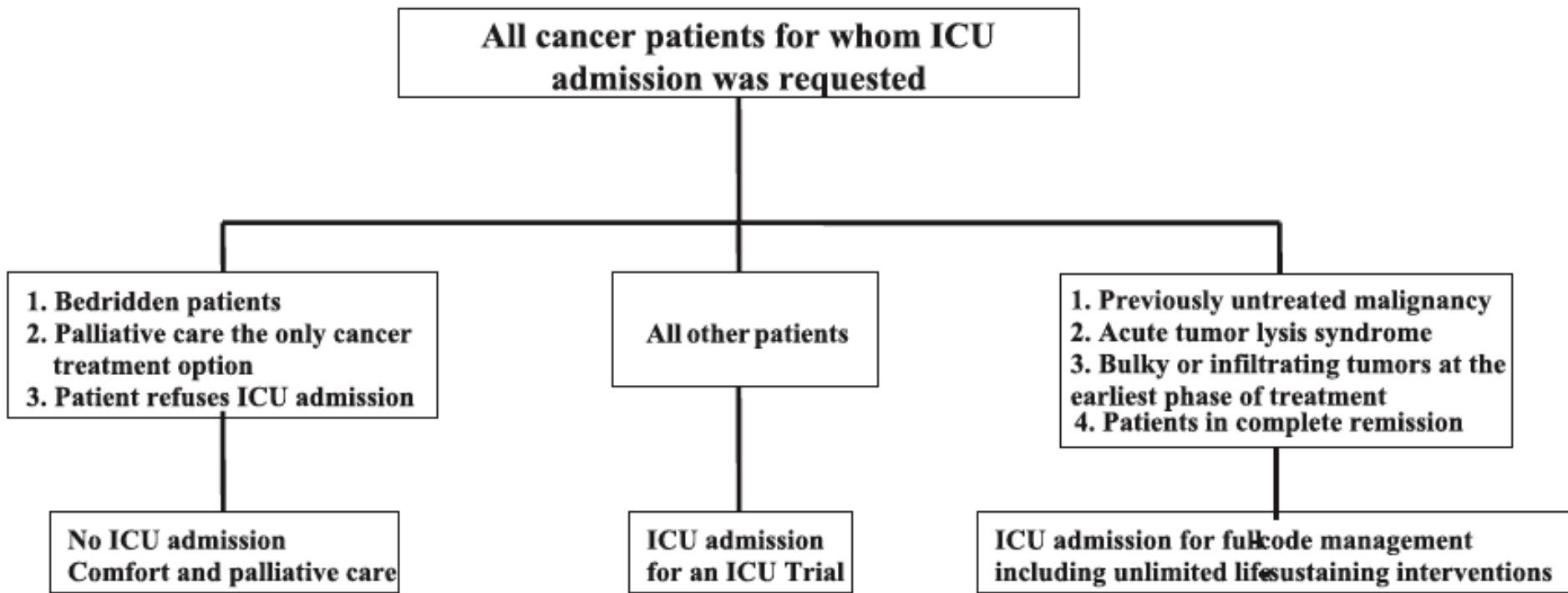
Acute myeloid leukemia and critical care...

Patients (n=):	83	
Intubated (%):	57	
Induction (prior or during; %):	68	
ICU mortality (%):	34	
ICU mortality if MV (%):	60	
ICU survivors alive at 1-y (%):	51	(= 34% of all pts.)
ICU survival depends on:	SAPS II and MV	
1-y survival depends on:	age, performance status, M3, CR	

Acute myeloid leukemia and critical care...

Patients (n=):	45
Proportion of all AML pts. (%):	13
Intubated (%):	67
De novo (%):	61
ICU mortality (%):	38
ICU mortality if MV (%):	70
Hospital mortality (%):	44
90-d mortality (%):	51
1-y mortality: (%):	71

ICU admission criteria for patients with malignancy



AML patients within the „ICU trial“

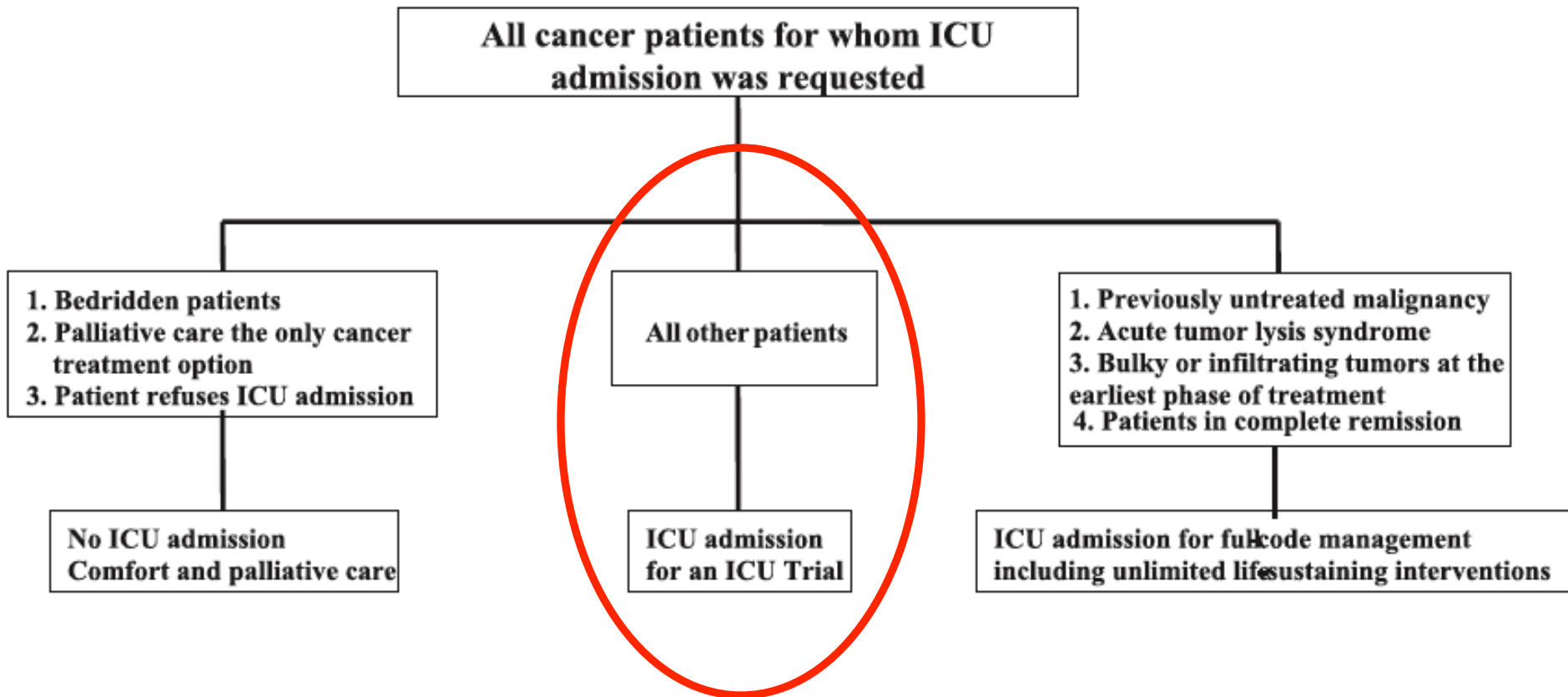


Table 1. Characteristics of the malignancy

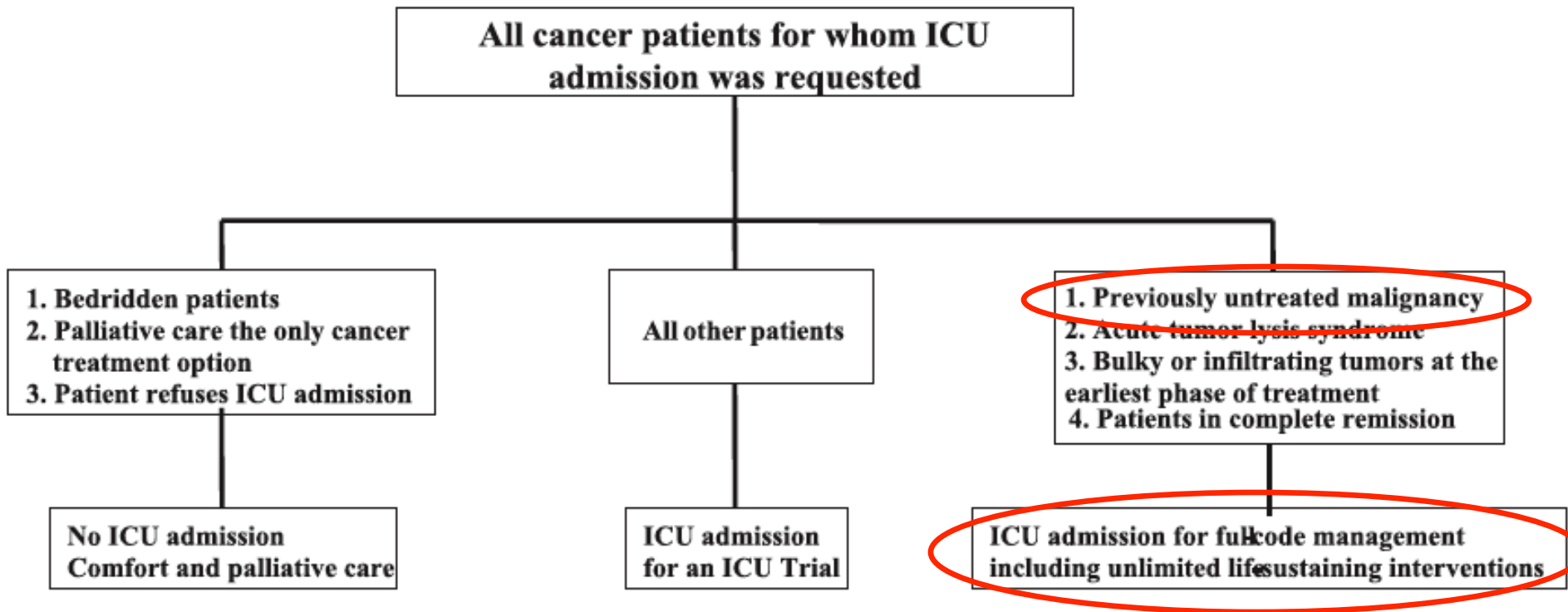
Patients	Early Decedents (n = 85)	Decedents After Day 4 (n = 62)	Hospital Survivors (n = 41)	p Value
Age, yrs (IQR)	51 (36–67)	56.8 (47.2–66.7)	44.7 (42.1–58.8)	.05
Male gender, n (%)	55 (64)	43 (69.3)	26 (63.4)	.6
Comorbidities, n (%)				
Hypertension	30 (35.3)	19 (30.6)	5 (12.1)	.03
COPD	8 (9.4)	7 (11.3)	6 (14.6)	.7
Chronic heart failure	4 (4.7)	3 (4.8)	2 (4.8)	.9
Long term steroids	1 (1.2)	3 (4.8)	3 (7.3)	.6
One comorbidity	29 (34.1)	35 (56.4)	19 (46.3)	.4
Chronic health status, n (%)				
Normal or slight alteration	74 (87.1)	49 (78.9)	32 (78)	.7
Altered	11 (12.9)	13 (20.9)	9 (21.9)	.9
Bedridden	0	0	0	—
Characteristics of the malignancy, n (%)				
Acute leukemia	25 (29.4)	20 (32.3)	11 (26.8)	.5
Chronic lymphocytic leukemia	5 (6)	3 (4.8)	2 (4.9)	.9
Non-Hodgkin's lymphoma	20 (23.5)	14 (22.6)	11 (26.8)	.6
Multiple myeloma	10 (11.8)	7 (11.3)	4 (9.7)	.8
Lung and breast cancer	12 (14.1)	8 (12.9)	6 (15.3)	.8
Other solid tumor	13 (15.3)	10 (16.1)	7 (17)	.9
Time from diagnosis, days (IQR)	54 (11–179)	37 (6–340)	67 (15–343)	.8
Treatments received for the malignancy				
Courses of chemotherapy, n (IQR)	3 (1–3)	2.5 (0–4)	3.3 (0–5.25)	.7
Autologous stem cell transplantation, n (%)	10 (11.7)	9 (14.5)	5 (12.9)	.8
Status of the malignancy at ICU admission, n (%)				
First 3 months of the treatment	45 (52.9)	36 (58)	23 (56)	.4
Remission or stability	40 (47.1)	21 (34)	16 (39)	.6
Relapse	0	4 (6.5)	2 (5)	.2

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Patients with AML: 56 pts.
 Early decedents: 45%
 Decedents > day 4: 36%
 Hospital survivors: 20%

ICU admission in *de novo* AML?



Impact of critical illness in *de novo* AML?

- Percentage of patients in need of ICU?
- Early factors predicting ICU admission?
- Effect of ICU on short and long term survival?
- Effect of ICU on hematologic outcome?

Design, Patients and Methods

Patients: all *de novo* AML pts. eligible for induction chemo

Design: retrospective cohort study, 12-year period

comparison ICU vs. non-ICU patients

Design, Patients and Methods

Patients: all *de novo* AML pts. eligible for induction chemo

Design: retrospective cohort study, 12-year period

comparison ICU vs. non-ICU patients

- Outcome:
- predictors for ICU admission
 - *independent* prognostic effects of the ICU on survival and on remission status (CCR)
 - „survival 30“

Induction therapy of AML

DAV protocol for all patients
(AIDA protocol for patients with M3)

Blast cell persistence?



MiDAC protocol for patients <60
DAV protocol for patients >60

Blast cell persistence?



FLAG protocol

ICU admission

- granted to all patients with *de novo* AML
- no specific admission policy
- decision taken by senior hematologist and intensivist

Design, Patients and Methods: Statistics

- Cox regression (survival)
- logistic regression (ICU admission and ICU outcome)
- Kaplan Meier (probability of survival, survival 30 and CCR)

Results

Total pat.-number:	406
Age:	59 (15-89)
ICU admission:	62 (15%)
Prior / during induction:	25 / 37 pts.
Median time to admission:	13 (0-97) days
SAPS II:	64 (30-107)
Invasive ventilation:	68%

Results

ICU mortality:	55%	
ICU mortality MV / no MV:	67% / 25%	
Median survival:	19.6 vs. 1.3 months	
Survival (8 years):	21 vs. 9%	(p<0.05)
Survival 30 (6 years):	28 vs. 20%	(p=n.s.)
CCR (6 years):	38 vs. 33%	(p=n.s.)

Epidemiology

Table 1. Patients' characteristics at diagnosis.

	All patients (n=406)	Non-ICU patients (n=344)	ICU patients (n=62)	P value
Age (years)	59 (15-98)	58 (16-89)	63 (19-86)	0.146
Sex (f/m; n)	199/207	169/175	30/32	0.914
WBC (x10 ⁹ /L)	12.5 (0.03-450)	11.5 (0.03-312.4)	22.4 (0.12-450)	0.027
Platelets (x10 ⁹ /L)	52 (2-1110)	50 (2-1110)	57 (10-320)	0.455
Hemoglobin (g/dL)	9.4 (4.8-14.8)	9.4 (4.8-14.8)	9.4 (5.8-14.1)	0.805
LDH (U/L)	389 (116-6820)	380 (116-6820)	478 (155-4000)	0.102
CRP (mg/dL)	3.9 (0.1-42.4)	3.0 (0.1-42.2)	7.0 (0.5-36.7)	<0.001
Fibrinogen (mg/dL)	413 (59-1020)	414 (59-1020)	399 (76-671)	0.067

Charlson Comorbidity Index

CCI risk groups	All patients (n=406) %	Non-ICU patients (n=344) %	ICU patients (n=62) %	P value
0	77.5	79.6	65.6	0.001
1-2	19.3	18.7	23.0	
3-4	2.7	1.5	9.8	
≥5	0.5	0.3	1.6	

Details on comorbidities

Table 4. Comorbidities in ICU and non-ICU patients.

Comorbidity	Non-ICU patients (n=344) frequency (%)	ICU patients (n=62) frequency (%)	P value
Myocardial infarction	10 (2.9)	2 (3.2)	0.570
→ Congestive heart failure	7 (2.0)	5 (8.1)	0.024 ←
Peripheral artery disease	3 (0.9)	1 (1.6)	0.486
→ Cerebral artery disease	5 (1.5)	4 (6.5)	0.034 ←
Dementia	1 (0.3)	0 (0.0)	1.000
Chronic obstructive lung disease	13 (3.8)	2 (3.2)	1.000
Collagenosis	1 (0.3)	0 (0.0)	1.000
Gastric ulcer	11 (3.2)	2 (3.2)	1.000
Liver cirrhosis	0 (0.0)	1 (1.6)	0.153
Diabetes mellitus			
without organ damage	14 (4.1)	6 (9.7)	0.101
with organ damage	6 (1.7)	1 (1.6)	1.000
→ Hemiplegia	3 (0.9)	3 (4.8)	0.048 ←
→ Chronic renal failure	1 (0.3)	5 (8.1)	<0.001 ←
Solid tumor	8 (2.3)	2 (3.2)	0.654

Infection at diagnosis

At the time of diagnosis	Non-ICU patients (n=344) (%)	ICU-patients (n=62) (%)
Clinical signs of infection	34	68
Focus of infection	16	34
Pulmonary infiltrate	10	24

Factors predicting ICU admission

Factors predicting ICU admission (n=406)	Univariate analysis Odds Ratio [95% CI]	Multivariate analysis Odds Ratio [95% CI]
White blood cell count	1.50 [1.04-2.17]	0.96 [0.55-1.69]
→ Fibrinogen	0.16 [0.05-0.57]	0.07 [0.02-0.24]
Lactate dehydrogenase	2.10 [0.90-4.87]	
C-reactive protein	2.98 [1.75-5.06]	1.57 [0.73-3.38]
FAB-subtype	not significant	
Karyotype	not significant	
→ Infection	4.11 [2.31-7.32]	3.80 [1.59-9.10]
Age	1.12 [0.95-1.31]	
→ Comorbidity (CCI)	2.07 [1.34-3.20]	2.17 [1.32-3.56]

Reasons for ICU admission

Table 2. Reason for ICU admission.

	All ICU patients (n=62) frequency (%)	ICU survivors (n=28) frequency (%)	ICU non-survivors (n=34) frequency (%)	<i>P</i> value
Respiratory failure	31 (50.0)	15 (53.6)	16 (47.1)	0.799
Severe bleeding	14 (22.6)	6 (21.4)	8 (23.5)	1.000
Sepsis	5 (8.1)	1 (3.6)	4 (11.8)	0.366
CPR	5 (8.1)	1 (3.6)	4 (11.8)	0.366
Postoperative admission	3 (4.8)	3 (10.7)	0 (0.0)	0.087
Acute renal failure	2 (3.2)	1 (3.6)	1 (2.9)	1.000
Acute myocardial infarction	1 (1.6)	0 (0.0)	1 (2.9)	1.000
Leukapheresis	1 (1.6)	1 (3.6)	0 (0.0)	0.452

Factors predicting ICU outcome

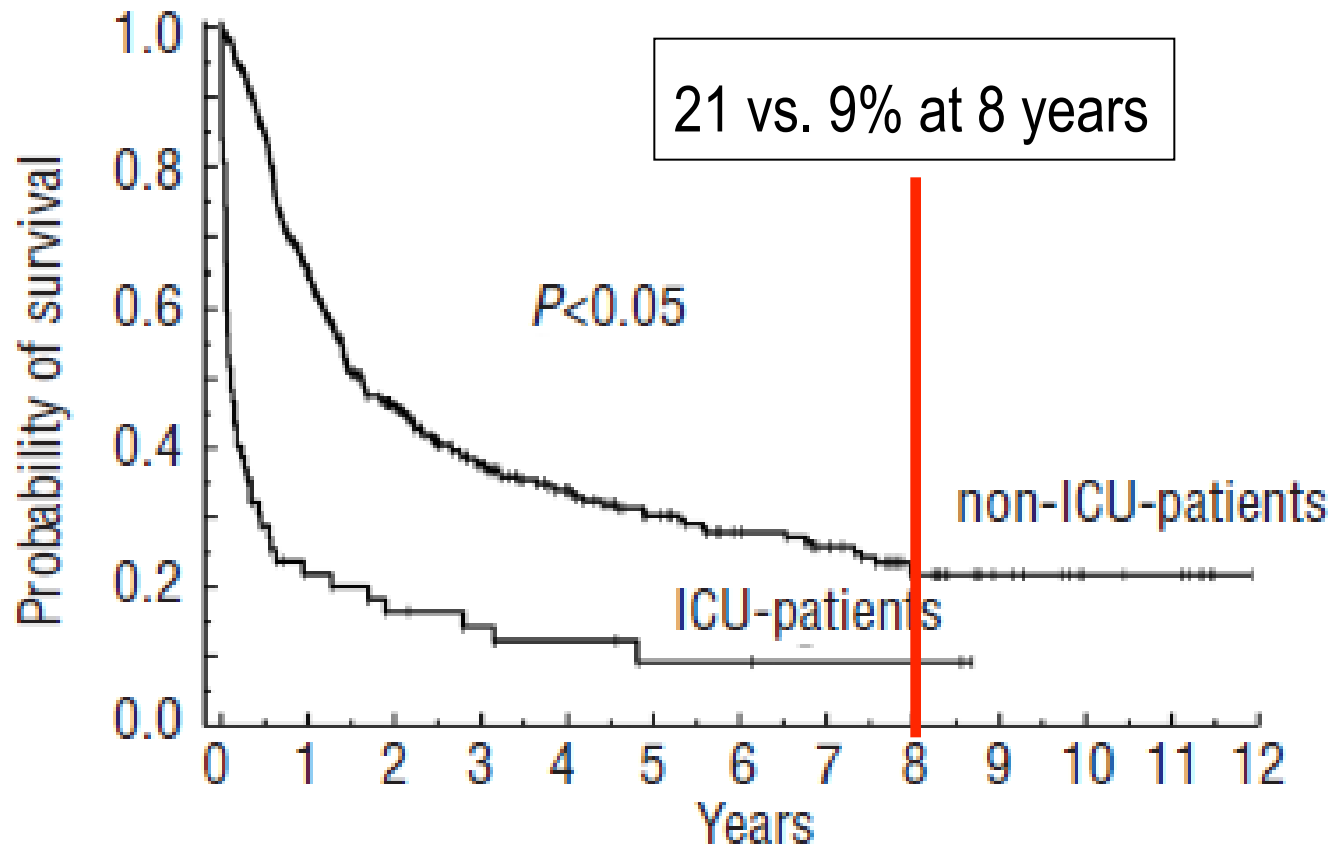
Factors predicting ICU outcome (n=62)	Odds Ratio [95% CI]	Odds Ratio [95% CI]
White blood cell count	0.96 [0.51-1.81]	
Fibrinogen	1.04 [0.12-8.87]	
C-reactive protein	2.50 [0.94-6.65]	
Invasive mechanical ventilation	0.25 [0.03-2.58]	
Vasopressor support	6.69 [2.01-22.33]	1.70 [0.34-8.35]
SAPS II	1.95 [1.30-2.91]	1.82 [1.17-2.83]
Time from diagnosis to admission	0.91 [0.73-1.13]	
Cause of admission	not significant	



Long term survival in ICU patients

Factors predicting long term survival in ICU patients (n=62)	Hazard Ratio [95%-CI]	Hazard Ratio [95%-CI]
Fibrinogen	0.57 [0.17-1.90]	
SAPS II	1.35 [1.15-1.59]	1.34 [1.13-1.58]
CCI	1.52 [1.06-2.16]	1.20 [0.80-1.80]
Karyotype	not significant	

Probability of long term survival

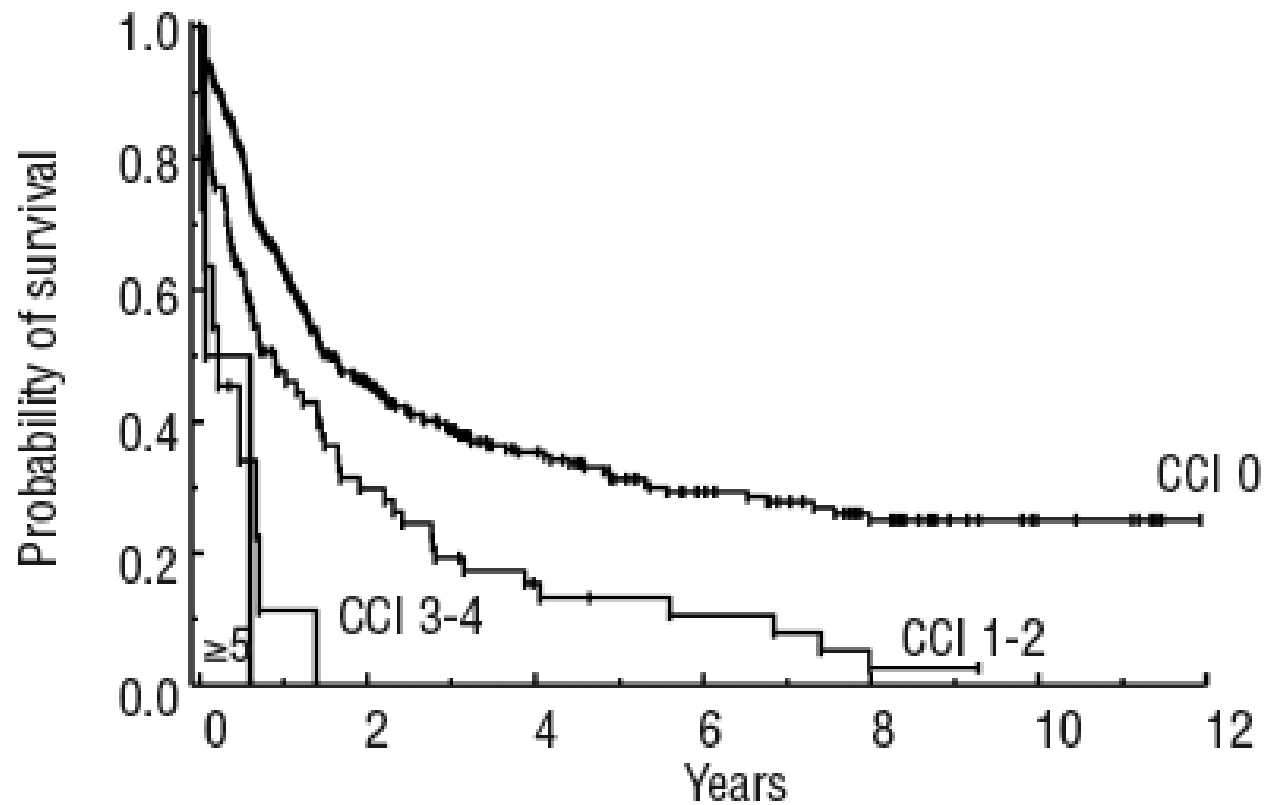


Probability of long term survival

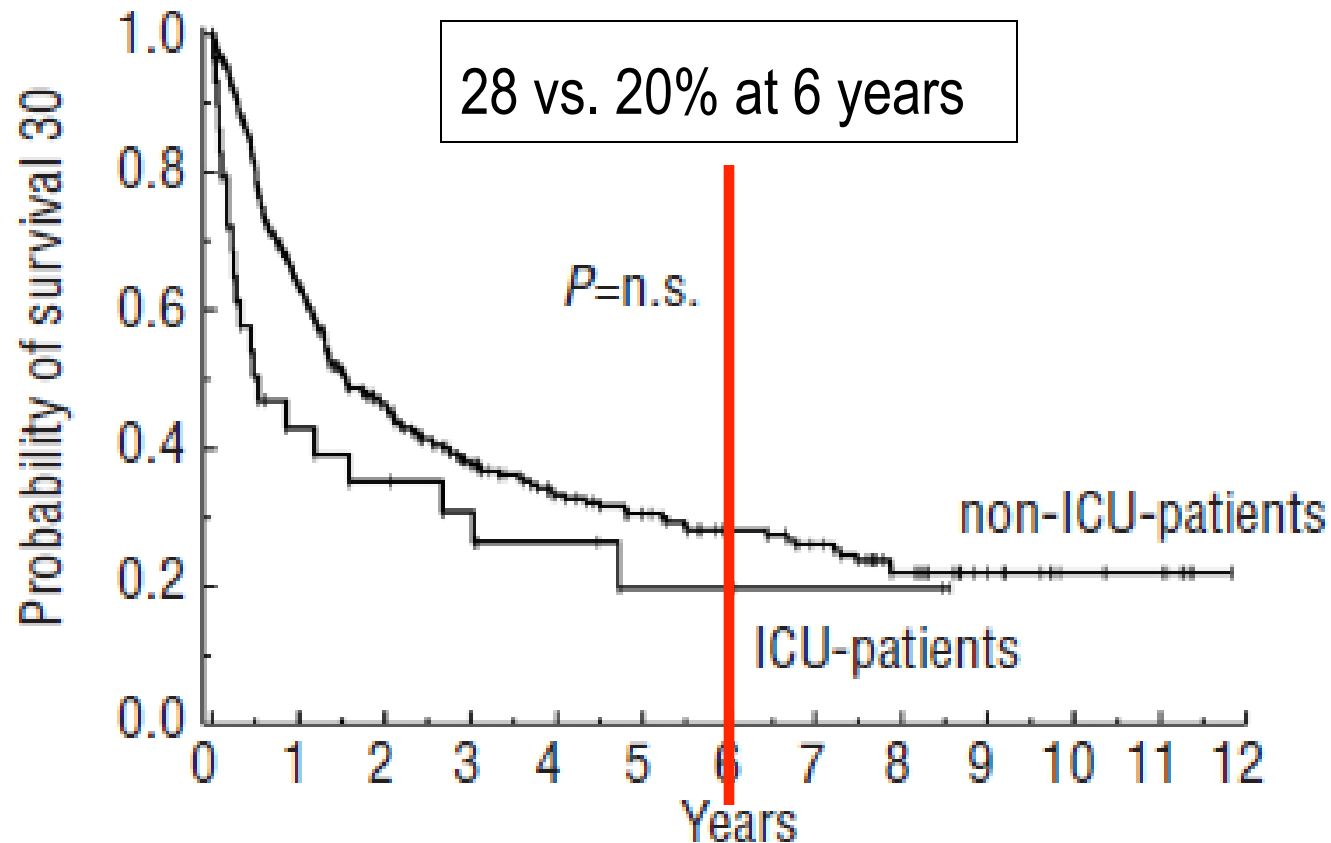
Independently associated with:

- ICU status
- Age
- Karyotype
- White blood count
- Lactate dehydrogenase
- Charlson comorbidity index

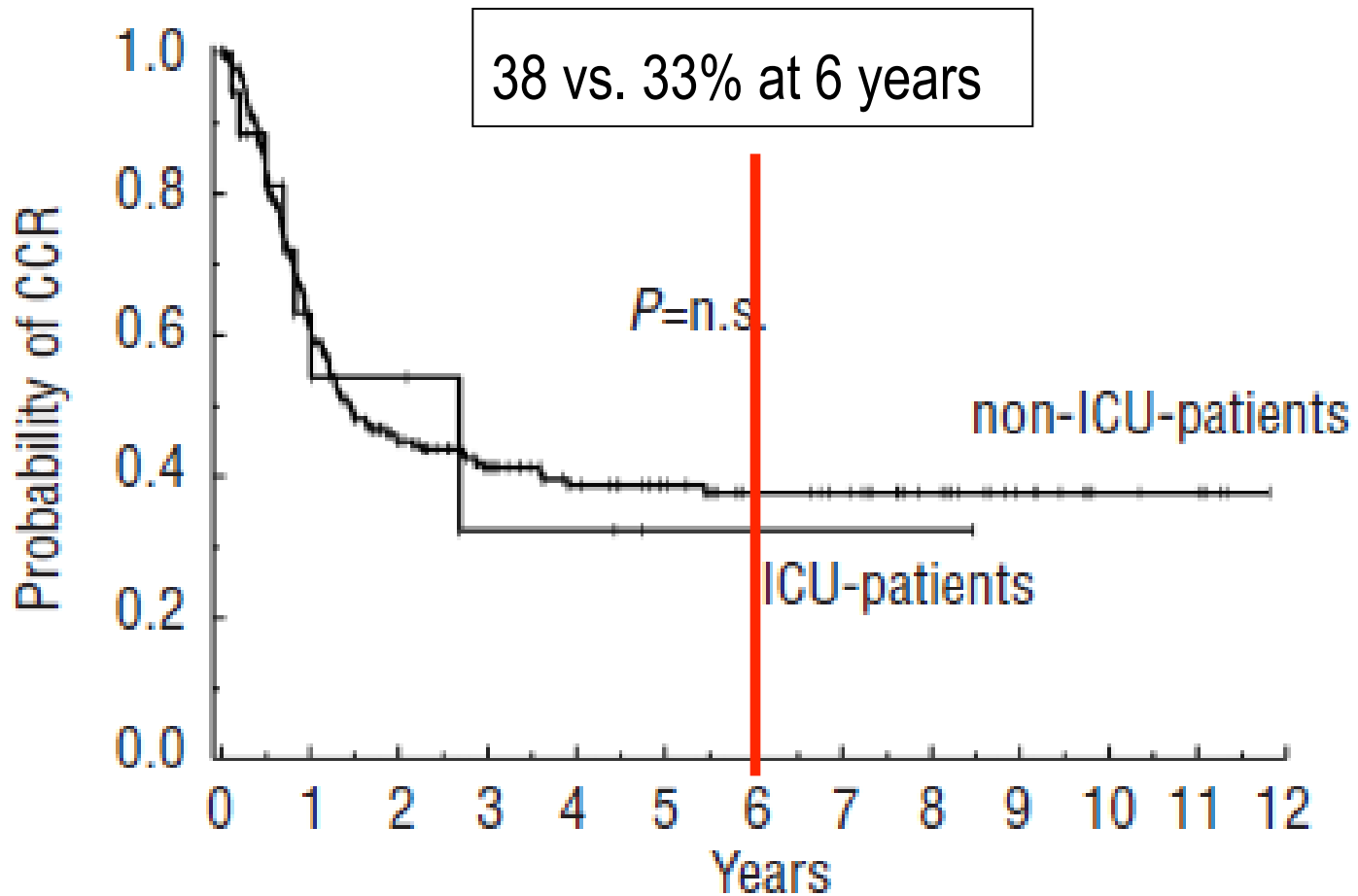
Probability of long term survival



Probability of survival 30



Probability of CCR



Conclusion I

ICU admission...

... is *frequent* in patients with *de novo* AML (15%)

... is mainly due to respiratory failure or bleeding

... is correlated with *parameters known at diagnosis*

- infection
- comorbidity
- fibrinogen↓

Conclusion II

ICU admission is a risk factor for adverse long term survival

But...

... *not* true in early phase survivors (survival 30) !

... ICU survival depends *exclusively* on SAPS II !

... hematologic outcome (CCR) *independent* from ICU status !

Prognostic factors for intensive care unit admission, intensive care outcome, and post-intensive care survival in patients with *de novo* acute myeloid leukemia: a single center experience

Peter Schellongowski,¹ Thomas Staudinger,¹ Michael Kundi,² Klaus Laczika,¹ Gottfried J. Locker,¹ Andja Bojic,¹ Oliver Robak,¹ Valentin Fuhrmann,³ Ulrich Jäger,⁴ Peter Valent,^{4,5} and Wolfgang R. Sperr^{1,4}

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Bring your patients with *de novo* AML to the ICU!

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