

Journal Club

高齢者のICU入院は 予後を改善させるのか？

2017/12/12

聖マリアンナ医科大学 救急医学

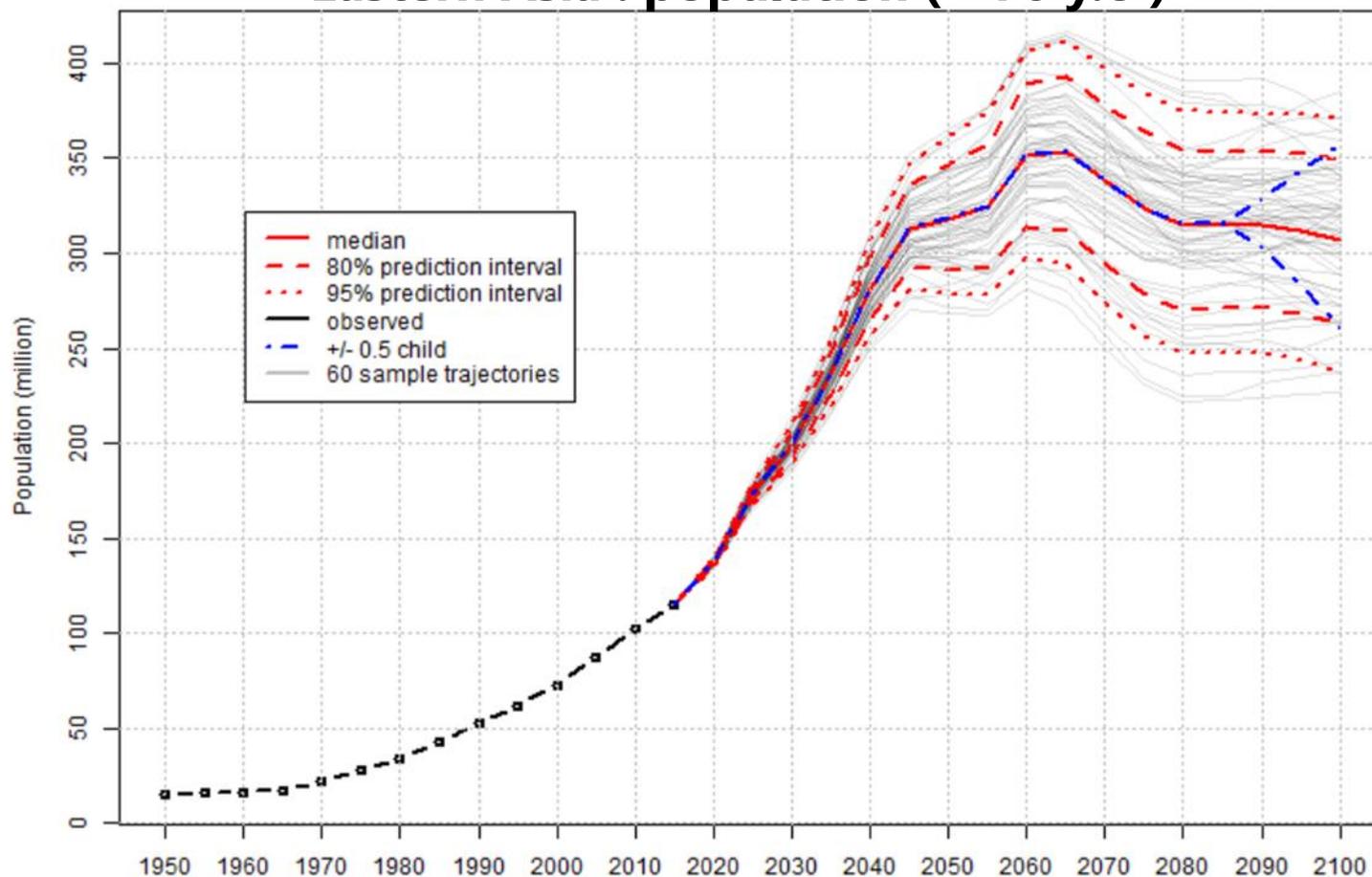
PGY4 原田佳奈

指導医 尾崎将之先生

Background

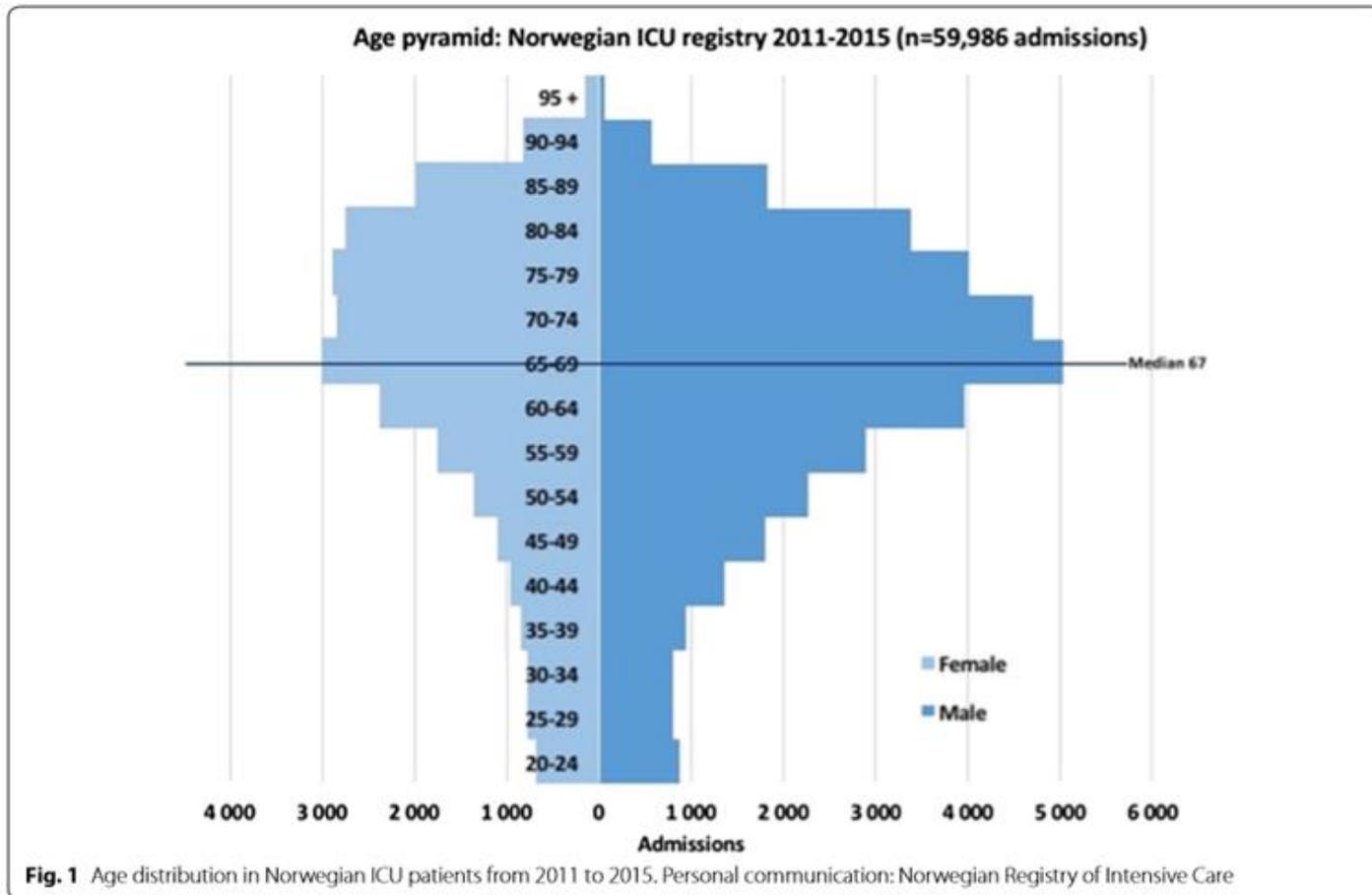
高齢者人口の推移

Eastern Asia : population (>70 y.o)



高齢者はどんどん増え続ける……

ICU入院の概要



ICU入院の平均年齢は65歳以上

Intensive Care Med. 2017;43(9):1319-1328

The status of intensive care medicine research and a future agenda for very old patients in the ICU

高齢者のICU入院は増加

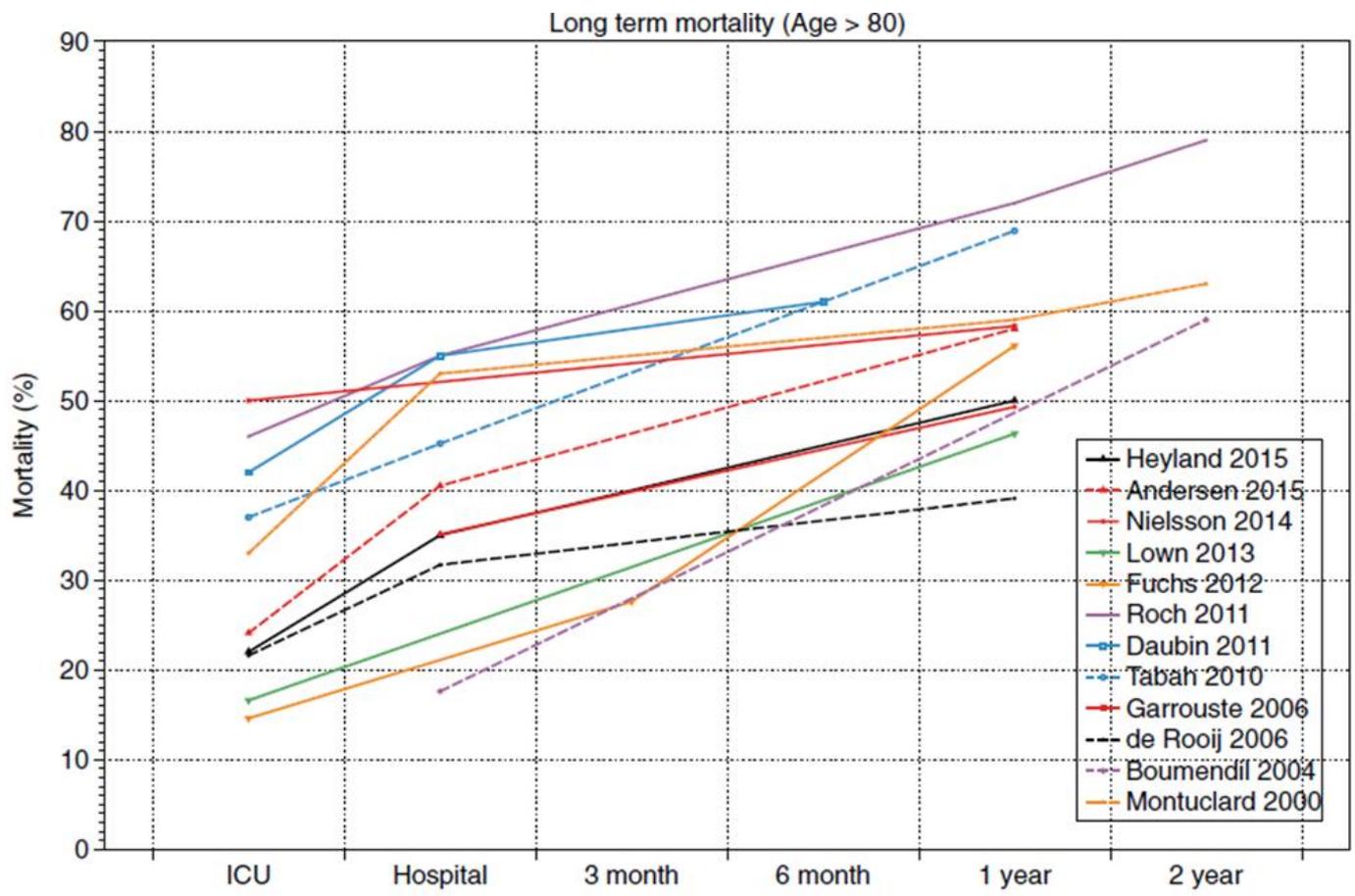
国	著者 発表年	数 (>80 y.o)	80歳以上の割合
Netherland	Haas 2015	39558	13.4→13.9%に増加
Denmark	Nielsson 2014	6266	11.7→13.8%に増加
Australia	Ihla 2012	17126	11.5→15.3%に増加
Australia & New Zealand	Bagshaw 2009	15640	1年5.6%増加

80歳以上のICU入院の割合は増加傾向

Intensive Care Med. 2017;43(9):1319-1328

The status of intensive care medicine reserch and a future agenda for very old patients in the ICU

入院した高齢者の予後

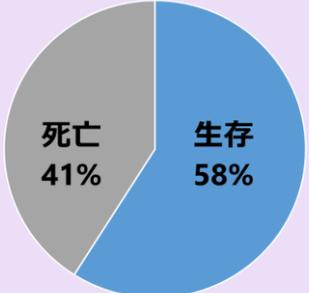
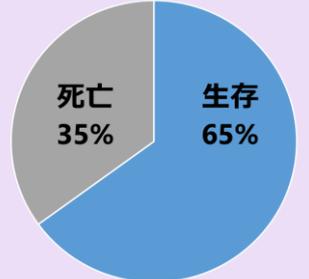


80歳以上の1年死亡率は40-70%

Intensive Care Med. 2017;43(9):1319-1328

The status of intensive care medicine reserch and a future agenda for very old patients in the ICU

高齢者のICU入院費用

費用計算の対象	ICU入院費用 (Canadian \$)	母集団
全患者	\$31,674	n = 1671 
ICUを生存して退院した患者	\$48,744	n = 610 
退院1年後まで追跡した患者	\$61,783	

Crit care. 2017;21(1):109

Cost analysis of the very elderly admitted to intensive care units.

高齢者のICU入院は望ましい？

医者への考えは様々

反対派

ICUに入院した高齢者の
1年死亡率40-70%

→予後が悪い高齢者に
ICU入院の費用を使うのは
医療費の浪費
病態の治療のみでなく、
QOLを重視すべき

賛成派

高齢者というだけで、
成人に比べて機械による
臓器サポートや薬物治療
が不十分な傾向がある

→成人と同様に、病態に
応じて必要な治療はする
べきである

高齢者のICU入院は望ましい？

一致した見解がないのは
高齢者のICU入院の適応に関する
確立した基準がないから！



ではどのような高齢者を
ICUに入院させるべき？

ICU CUB 1 study

80歳以上の救急外来患者を対象とした 初めての前向き研究

Selection of intensive care unit admission criteria for patients aged 80 years and over and compliance of emergency and intensive care unit physicians with the selected criteria: An observational, multicenter, prospective study*

Maité Garrouste-Orgeas, MD; Ariane Boumendil, PhD; Dominique Pateron, MD; Philippe Aegerter, MD, PhD; Dominique Somme, MD; Tabassome Simon, MD, PhD; Bertrand Guidet, MD; on behalf of the ICE-CUB Group

ICU CUB 1 study

* 高齢者向けのICU入院基準を作成

* 以下の4点を調査

- ①ICU入院は実際何%いたのか？
- ②ICU入院に寄与した因子は？
- ③予後良好な患者の特徴は？
- ④ICU入院を要した患者は実際何%？

高齢者向けのICU入院基準の作成

ICU入院のcriteria 74項目
(1999年 Society of Critical Care Medicine)
↓
76項目に修正
(17項目削除、6項目修正、22項目追加)

30人の救急医が全項目を
criteriaとしてふさわしいか選定
→3回繰り返す

44項目 : definitive

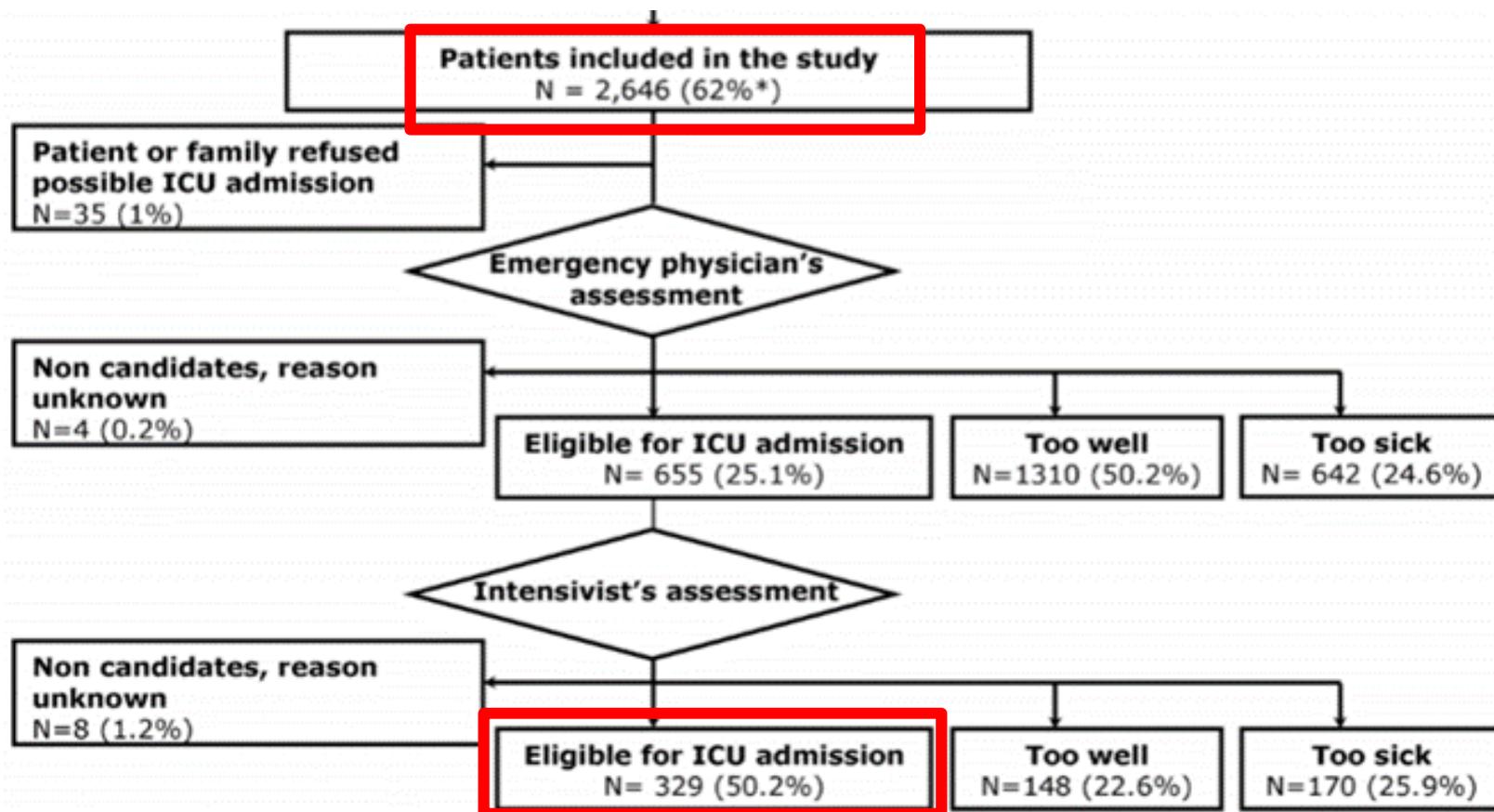
30項目 : equivocal

ICU入院が望ましい病態(table1)

	数	%	ICU 入院率	入院中 死亡率	6か月 死亡率
循環					
心原性ショック	44	3.6	25%	53.5%	70.4%
出血性ショック	12	1.0	66.7	33.3	66.7
急性心不全(強心薬や人工呼吸必要)	78	6.4	7.7	18.0	46.1
急性心不全(NIPPV)	98	8.0	15.3	25.5	50.0
中毒					
薬物中毒	41	3.3	14.6	5.0	21.9
自殺企図	9	0.7	22.2	11.1	22.2
手術					
術前に循環/呼吸補助が必要 侵襲的monitoringが必要	22	1.8	31.8	40.9	59
神経					
意識/呼吸障害のある中枢性神経疾患	10	0.8	10.0	60.0	80.0
中毒による意識障害	9	0.7	0	44.4	66.7

	数	%	ICU 入院率	入院中 死亡率	6か月 死亡率
消化器					
消化管出血	57	4.6	21.0	12.2	33.3
消化管出血(循環障害あり)	31	2.5	25.8	19.3	35.4
呼吸					
COPD急性増悪	200	16.3	12.5	18.0	42.0
肺塞栓症	84	6.8	9.5	13.1	25.0
緊急挿管が必要な呼吸不全	30	2.4	30.0	66.7	76.7
挿管が必要な呼吸不全	39	3.2	41.0	56.4	71.8
NIPPVが必要な呼吸不全	85	6.9	22.3	29.4	50.6
重症肺炎	136	11.1	19.8	27.9	51.5
その他					
敗血症性ショック	157	12.8	14.1	58.5	76.4
RRTが必要な急性腎不全	27	2.2	48.1	33.3	59.2
低血圧(sBP<80)	58	4.7	8.6	34.4	56.8
合計	1227		17.9	30.5	51.3

①ICU入院は実際何%いたのか？



たった**12%**(329/2646人)！
(5－38%と施設間でばらつきあり)

②ICU入院に寄与した因子は？

	OR/year	95% CI
年齢	0.91	0.87-0.94
疾患の重症度	Point score MPM ₀ 1.77	1.51-2.08
患者の自立度	ADL score 1.32	1.19-1.46
活動的な癌	0.60	0.33-1.05
栄養	Preserved vs poor 0.42	0.20-0.82
向精神病薬	0.66	0.45-0.95

低年齢、疾患が重症、ADLが低い、
栄養状態が悪い、向精神病薬が少ないほど
ICU入院が多い

③ 予後良好な患者の特徴は？

ADLがよい
栄養状態がよい
活動的な癌がない

6か月死亡率

上記を満たす	31%
満たさない	63%

④ICU入院を要した患者は実際何%？

Table1より、**1227/2646人(46%)**

そのうちのICU入院に適した(=予後が良い)患者
560人の中で実際に入院した患者は**23%**のみ

→予後の良い高齢者たちをICUに入院
させないでいる現状があるのではないか！
それはもったいない！

Clinical Question

予後の良い高齢者たちをICUに入院するように積極的に働きかけた場合、死亡率を改善させるのではないか??

Research

JAMA | **Original Investigation** | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Systematic Intensive Care Unit Triage on Long-term Mortality Among Critically Ill Elderly Patients in France A Randomized Clinical Trial

Bertrand Guidet, MD; Guillaume Leblanc, MD; Tabassome Simon, MD, PhD; Maguy Woimant, MD;
Jean-Pierre Quenot, MD; Olivier Ganansia, MD; Maxime Maignan, MD; Youri Yordanov, MD; Samuel Delerme, MD;
Benoit Doumenc, MD; Muriel Fartoukh, MD; Pierre Charestan, MD; Pauline Trognon, MD; Bertrand Galichon, MD;
Nicolas Javaud, MD; Anabela Patzak, MD; Maité Garrouste-Orgeas, MD; Caroline Thomas, MD;
Sylvie Azerad, PharmD; Dominique Pateron, MD; Ariane Boumendil, PhD; for the ICE-CUB 2 Study Network

JAMA. 2017;318(15):1450-1459

本日の論文

P	75歳以上の救急外来受診患者
I	ICU入院を積極的に推奨する
C	今までと同様にICU入院を判断
O	Primary outcome 6か月後の全死亡率 Secondary outcome ICU入院率 病院内での死亡率 6か月後のADL 6か月後のQOL

Method

Participant selection

Inclusion criteria

75歳以上の救急外来受診患者で以下をすべて満たす
臓器補助を要する重症な状態が1つ以上ある(table1)
機能状態がよい(index of ADL score ≥ 4)
栄養状態がよい(医師がbedsideで判断)
活動的な癌がない

Exclusion criteria

24時間以上救急外来に滞在
研究参加への拒否

割り当て

Cluster RCT

それぞれの病院を最小単位として割り当て

the control group : Standard Practice

従来の方法でICUに入院させるか決定

the intervention group : Systematic Strategy

criteriaを満たした患者を

積極的にICUに入院させるように働きかける

割り当て

具体的な介入方法

<介入内容の普及>

- ICUへの系統だった入院の良さを院報で通達
- criteria を満たす患者の積極的入院を推奨する冊子やポスターを発行

割り当て

具体的な介入方法

<研究者を含めた会議を開催>

- ・ 研究開始前に会議を設け積極的入院を推奨
- ・ 毎月会議を開催(臨床研究医が企画)

全救急医、集中治療医が参加

全救急医、集中治療医にICU入院を再度推奨
登録された症例とその経過について討論

割り当て

具体的な介入方法

<criteriaを満たす患者の決定>

- ・ 救急医と集中治療医の双方で相談し criteriaを満たすか判断する
- ・ criteriaを満たした患者がいた場合、救急医は集中治療医に伝え、集中治療医がbedsideで患者を評価する

最終判断はそれぞれ医療チームで判断する

データ収集

Part1

• 初療時の評価

Part2

• 入院時の評価

Part3

• 6か月後の評価

データ収集

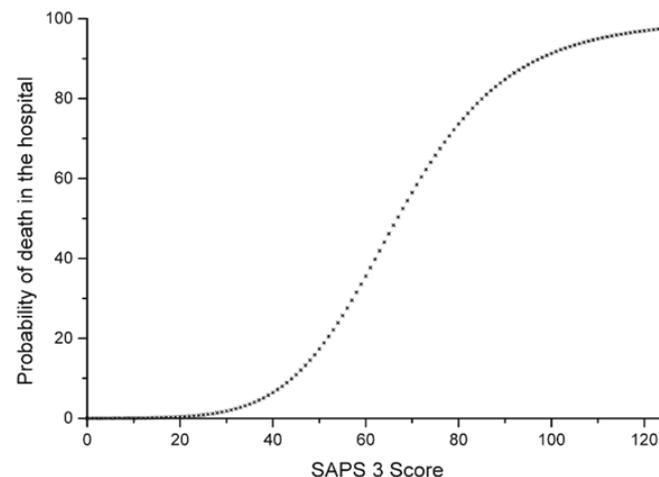
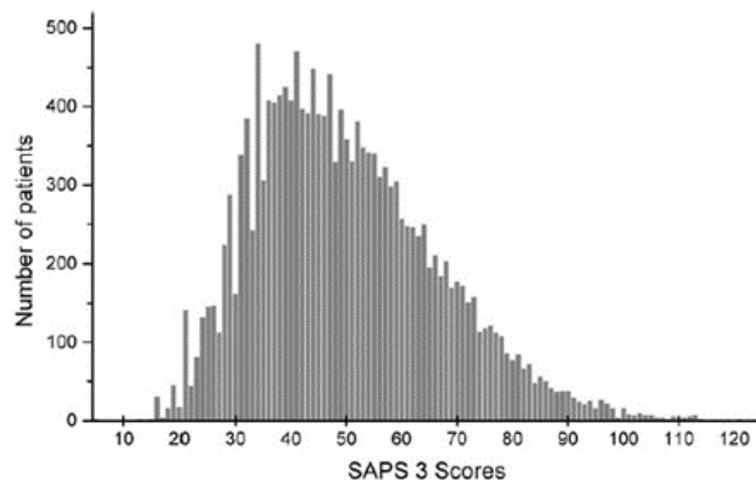
Part1 初療時の評価と入院までの経緯

- 救急外来受診の日時
- 年齢
- 性別
- 主病名
- SAPT3 score
- TYM score
- index of ADL
- 既往歴
- 生活拠点(家、施設、他)
- 生活環境(独居、夫婦、他)
- 患者のICUへの入院希望
- ICU bedの空き
- ICU入院に対する救急医、集中治療医の意見
- ICU入院の日時
- 患者が入院した科、日時

SAPS 3 score

ICU入院時における予後予測scoring
入院時の状態から、退院時の状態、予後を予測

Part I ~ IIIの3部構成で合計点を計算
理論上は0-217点(論文の分布は5-124点)



Intensive Care Med. 2005;31(10):1345-1355

SAPS 3-from evaluation of the patient to evaluation of the intensive care unit.
Part 2: development of a prognostic model for hospital mortality at ICU admission.

TYM score (自己記入式の認知機能評価)

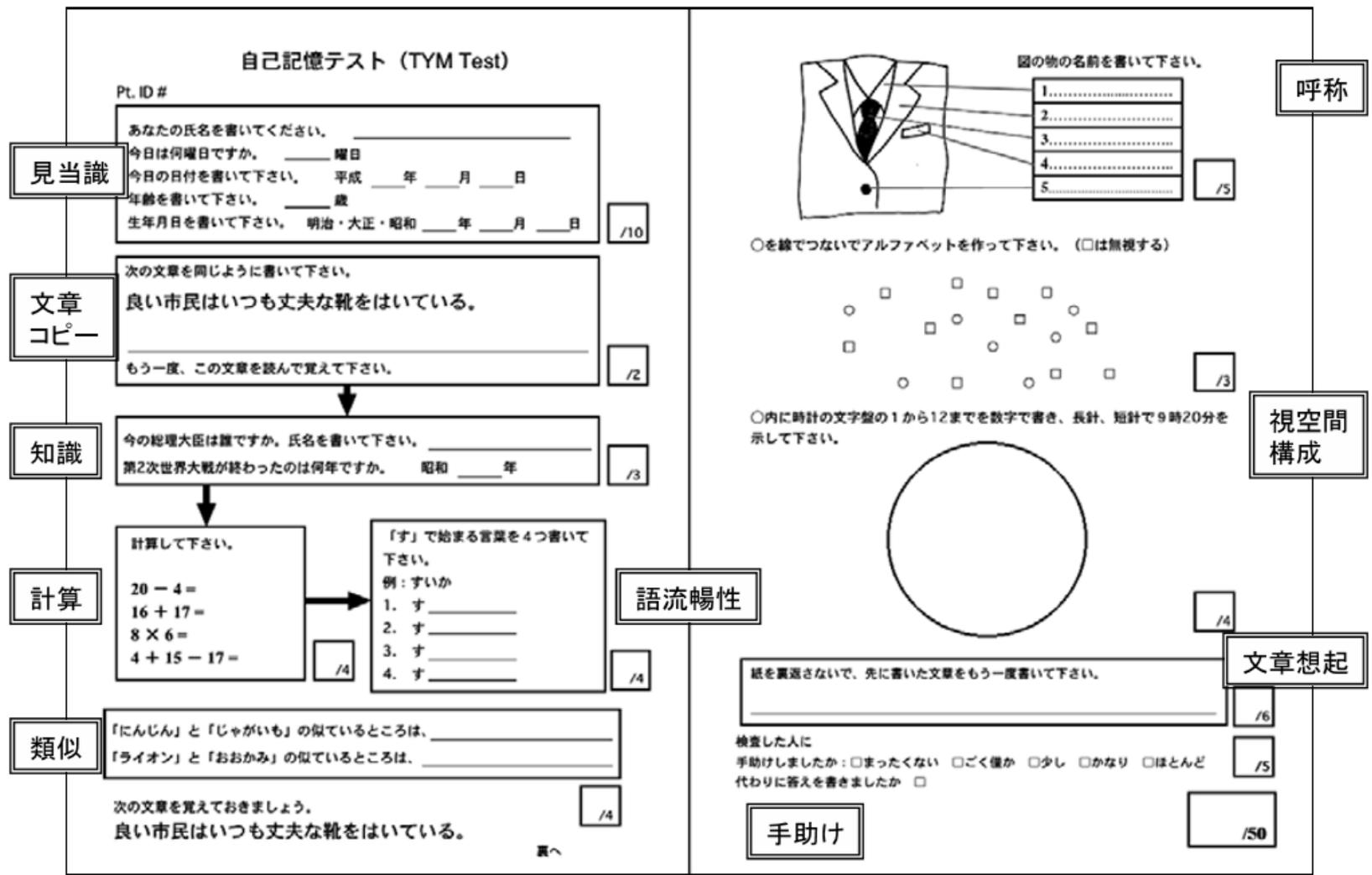


図1 社団法人京都保健会盛林診療所所長 / 社団法人認知症の人と家族の会顧問三宅貴夫の作成した日本語版のTYM (TYM-J)⁵⁾ (一部改変)

データ収集

Part2 全患者の入院中の経過

- 患者が入院していた最初の3つの科
- 退院日と退院時の状態
- 入院中の死亡日

Part3 6か月後の評価(研究医が電話でデータ収集)

- 生活の場所と生活様式
- Index of ADL
- QOL (SF-12)
- ここ6か月間での入院
- 介護者の負担 (ZARIT scale)

Index of Independence in ADL Score

Table 1.
Katz Index of Independence in Activities of Daily Living

Activities Points (1 or 0)	Independence (1 Point) NO supervision, direction, or personal assistance needed.	Dependence (0 Points) WITH supervision, direction, personal assistance, or total care.
BATHING Points: _____	(1 POINT) Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area, or disabled extremity.	(0 POINTS) Need help with bathing more than one part of the body, or getting in or out of the tub or shower. Requires total bathing.
DRESSING Points: _____	(1 POINT) Get clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	(0 POINTS) Needs help with dressing self or needs to be completely dressed.
TOILETING Points: _____	(1 POINT) Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.	(0 POINTS) Needs help transferring to the toilet, cleaning self or uses bedpan or commode.
TRANSFERRING Points: _____	(1 POINT) Moves in and out of bed or chair unassisted. Mechanical transfer aids are acceptable.	(0 POINTS) Needs help in moving from bed to chair or requires a complete transfer.
CONTINENCE Points: _____	(1 POINT) Exercises complete self-control over urination and defecation.	(0 POINTS) Is partially or totally incontinent of bowel or bladder.
FEEDING Points: _____	(1 POINT) Gets food from plate into mouth without help. Preparation of food may be done by another person.	(0 POINTS) Needs partial or total help with feeding or requires parenteral feeding.
Total Points: _____		

Score of 6 = High; patient is independent. Score of 0 = Low; patient is very dependent.

Slightly adapted from Katz S, Down TD, Cash HR, Grotz RC. Progress in the development of the index of ADL. *Gerontologist*. 1970;10(1):20-30.
Copyright © The Gerontological Society of America. Reproduced [Adapted] by permission of the publisher.

Katz index of ADL

ADLのscoring

- ①入浴、②更衣
③トイレ、④移動
⑤排泄、⑥食事

合計6点

0点：完全自立

6点：依存

JAMA.1963;185:914-919 Studies of illness in the aged:the index of ADL:
a standardized measure of biological and psychosocial function.

SF-12 Health Survey

- 12個の質問からQOLを計算
- 0-100点 (国民標準値50点、標準偏差10点)
- 8つの下位尺度より、身体的側面、精神的側面、役割/社会的側面を表す3つのscoreを算出

1. In general, would you say your health is:

₁ Excellent

₂ Very good

₃ Good

₄ Fair

₅ Poor

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

12. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

₁ All of the time

₂ Most of the time

₃ Some of the time

₄ A little of the time

₅ None of the time

ZARIT scale

Question	Score
1 Do you feel that your relative asks for more help than he/she needs?	0 1 2 3 4
2 Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?	0 1 2 3 4
3 Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?	0 1 2 3 4
4 Do you feel embarrassed over your relative's behaviour?	0 1 2 3 4
5 Do you feel angry when you are around your relative?	0 1 2 3 4
6 Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?	0 1 2 3 4
7 Are you afraid what the future holds for your relative?	0 1 2 3 4
8 Do you feel your relative is dependent on you?	0 1 2 3 4
18 Do you wish you could leave the care of your relative to someone else?	0 1 2 3 4
19 Do you feel uncertain about what to do about your relative?	0 1 2 3 4
20 Do you feel you should be doing more for your relative?	0 1 2 3 4
21 Do you feel you could do a better job in caring for your relative?	0 1 2 3 4
22 Overall, how burdened do you feel in caring for your relative?	0 1 2 3 4

0: NEVER
 1: RARELY
 2: SOMETIMES
 3: QUITE FREQUENTLY
 4: NEARLY ALWAYS

Interpretation of Score:

0 - 21 little or no burden
 21 - 40 mild to moderate burden
 41 - 60 moderate to severe burden
 61 - 88 severe burden

22項目からなる介護者の負担を数値化したもの

Method その他

* 研究期間

患者追跡期間：6か月間

登録期間：2年間

全期間：3年間

* Safety assessment

いかなる有害事象もadverse eventとして

カウントしたが、本研究ではとくに認めなかった

* 倫理的配慮

研究の概要についての情報を配布しICを得た

解析方法

* sample size

ICE-CUB1 studyより、75歳以上の救急外来受診患者の6か月死亡率が32%と推測。

6か月死亡率を6%下げようとして介入すると仮定。

ICC0.01とし、95%の両側検定をした場合、検定力74%で示すには2802人必要。

* baseline characteristics

連続変数はt検定で、

カテゴリー変数は χ^2 やFisher検定で評価

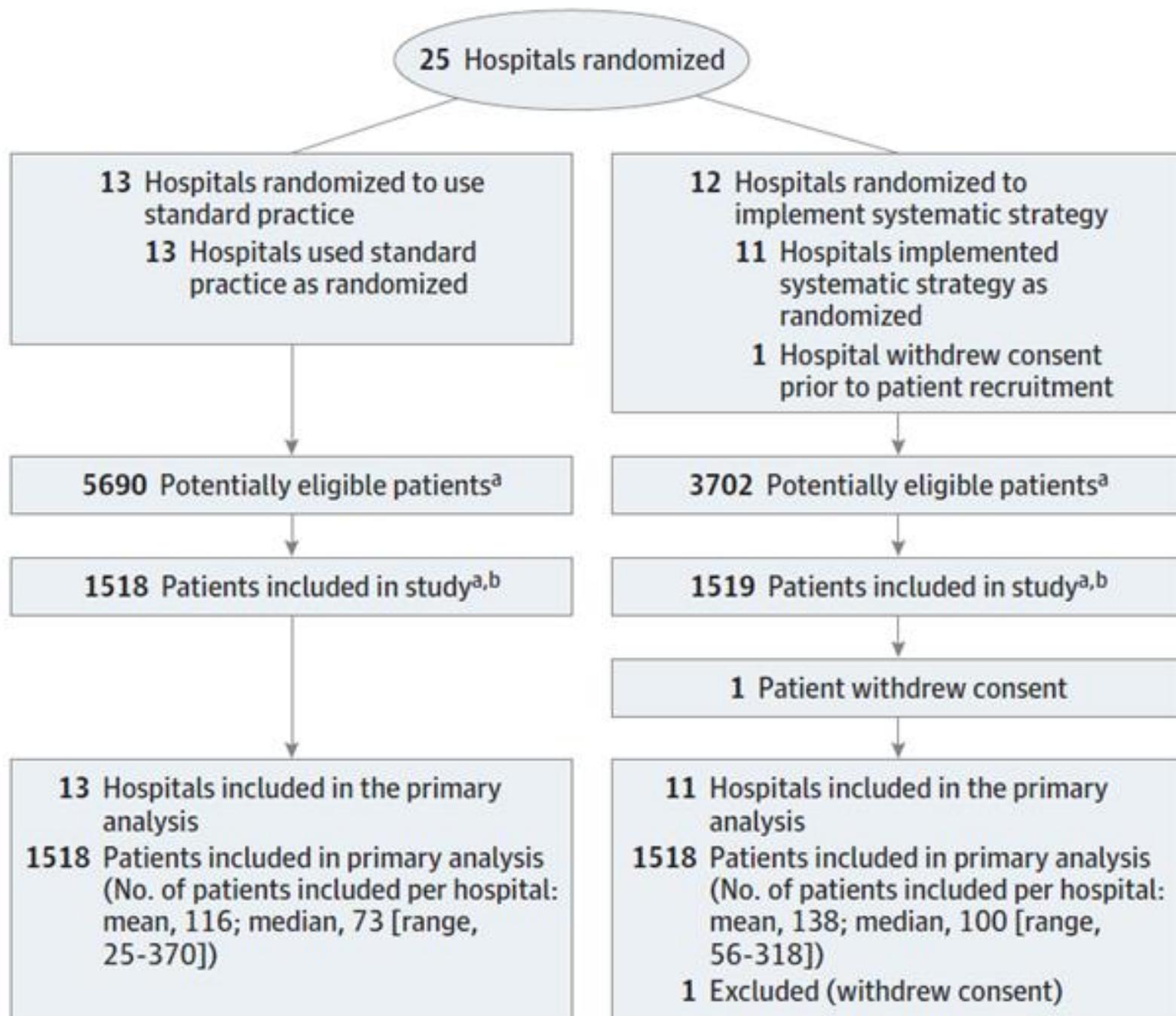
* binary outcome

ロジスティック回帰モデルで解析

解析方法

- * 6か月生存曲線はKaplan-Meier法で推測
baselineの補正はCox modelを使用し推測
- * ITT解析を施行
- * 中間解析は施行せず
- * 事後解析
それぞれの群でのICU入院となった患者の特徴を調査
- * 全解析は両側検定で $\alpha=0.05$ 、 $P<0.05$ で有意差ありと判断

Outcome



Baseline characteristics

Characteristics	Systematic Strategy	Standard Practice	Difference in Medians (95% CI)	P Value
Hospital characteristics	n=11	n=13		
No. of emergency department visits among patients aged >75 y during the study period, mean (SD)	12 746 (4402)	16 580 (9468)		
Location (Paris region), No.	7	9		
Geriatric ward in the hospital, No.	10	11		
Academic hospital, No.	7	10		
Type of intensive care unit (medical), No.	5	7		
Patient characteristics	n=1518	n=1518		
Age, median (IQR), y	85 (81-89)	85 (81-89)	0 (-1 to 1)	.60
Male, No. (%)	713 (47)	648 (43)		
Coexisting conditions, No./total No. (%)				
Ischemic heart disease or hypertension	397/978 (41)	456/1075 (42)		.40
Respiratory disorder	296/978 (30)	336/1074 (31)		.64
Congestive heart failure	151/978 (15)	119/1074 (11)		.004
Neurologic disorder	112/979 (11)	110/1075 (10)		.38
Cognitive impairment	100/977 (10)	153/1075 (14)		.006
Cirrhosis	16/979 (2)	16/1075 (1)		.79

Baseline characteristics

Characteristics	Systematic Strategy	Standard Practice	Difference in Medians (95% CI)	P Value
SAPS 3 score at enrollment, median (IQR) ^b	64 (57-71)	59 (54-65)	5 (4 to 6)	<.001
Index of Independence in ADLs score, median (IQR) ^c	6.0 (5.0-6.0)	6.0 (5.5-6.0)	0 (0 to 0)	.19
Initial clinical diagnosis, No. (%) ^d				
Respiratory failure	488 (32)	491 (32)		
Shock	320 (21)	238 (16)		
Cardiac disorder	177 (12)	231 (15)		
Coma	187 (12)	132 (9)		
Gastrointestinal tract disorder	57 (4)	117 (8)		<.001
Acute kidney failure	86 (6)	61 (4)		
Surgery	26 (2)	36 (2)		
Multiple trauma without surgery	10 (1)	9 (1)		
Other	165 (11)	202 (13)		

Systematic strategy の方が重症患者が多い

Baseline characteristics

	Systematic strategy (N=1,518)	Standard strategy (N=1,518)
Cardiac disorder		
Congestive heart failure requiring NIV	87 (6)	131 (9)
Arrhythmia	45 (3)	54 (4)
Cardiogenic shock	45 (3)	46 (3)
Surgery		
Gastrointestinal	15 (1)	22 (1)
Neurosurgery	3 (0.2)	6 (0.4)
Cardiac	3 (0.2)	2 (0.1)
Multiple traumatic injuries	1 (0.1)	2 (0.1)
Others	4 (0.3)	4 (0.3)
Coma		
Stroke	65 (4)	64 (4)
Metabolic	32 (2)	15 (1)
Status epilepticus	27 (2)	13 (1)
Toxic	16 (1)	14 (1)
Intracranial hypertension	11 (1)	18 (1)
Anoxic	24 (2)	1 (0.1)
Trauma	12 (1)	7 (0.5)
Respiratory disorder		
Chronic obstructive pulmonary disease	71 (5)	109 (7)
Pulmonary embolism	26 (2)	48 (3)
Severe pneumonia requiring high oxygen supply	105 (7)	145 (10)
Acute respiratory failure requiring mechanical ventilation	57 (4)	32 (2)
Acute respiratory failure requiring NIV	209 (14)	138 (9)
Acute respiratory failure requiring physiotherapy	20 (1)	19 (1)

	Systematic strategy (N=1,518)	Standard strategy (N=1,518)
Gastrointestinal tract hemorrhage	40 (3)	57 (4)
Pancreatitis	3 (0.2)	14 (1)
Acute liver insufficiency	0 (0)	5 (0.3)
Abdominal emergency	14 (1)	41 (3)
Renal		
Acute kidney failure	86 (6)	61 (4)
Shock		
Septic	244 (16)	169 (11)
Hemorrhagic	35 (2)	21 (1)
Hypovolemic	30 (2)	32 (2)
Others	11 (1)	16 (1)
Multiple traumatic injuries without surgery	10 (1)	9 (1)
Others	165 (11)	202 (13)

ICU入院が推奨される
病態ごとのそれぞれの数

Characteristics of the triage process

Characteristics	No./Total No. (%)		P Value
	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	
No empty ICU beds	241/1276 (19)	92/492 (19)	.98
Physician sought participant's opinion about ICU admissions			
Yes	470/1518 (31)	220/1518 (14)	<.001
No	326/1518 (21)	155/1518 (10)	
Patient unable to formulate opinion	438/1518 (29)	190/1518 (13)	
Not documented	284/1518 (19)	953/1518 (63)	
Participant opinion about ICU admission			
Favorable	414/470 (88)	145/220 (66)	<.001
Unfavorable	21/470 (5)	32/220 (15)	
No opinion	35/470 (7)	43/220 (20)	
Physician sought family's opinion about ICU admission			
Yes	517/1518 (34)	233/1518 (15)	<.001
No	337/1518 (22)	155/1518 (10)	
Not present or could not be reached	199/1518 (13)	93/1518 (6)	
Not documented	465/1518 (31)	1037/1518 (68)	
Family's opinion about ICU admission ^a			
Favorable	421/514 (82)	132/232 (57)	<.001
Unfavorable	69/514 (13)	71/232 (30)	
No opinion	24/514 (5)	29/232 (13)	

どちらもICU bedの空きがない場合が19%もある
 医者も患者も家族もsystematic StrategyがICU入院を多く希望

Characteristics of the triage process

Characteristics	No./Total No. (%)		P Value
	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	
Decision about admission destination ^b			
ICU in the same hospital	856/1513 (57)	458/1497 (31)	<.001
ICU in another hospital	75/1513 (5)	58/1497 (4)	
Intermediate care or specialized unit	242/1513 (16)	319/1497 (21)	
Other ward	104/1513 (7)	369/1497 (25)	
Post-emergency department unit	189/1513 (12)	261/1497 (17)	
Geriatric unit	17/1513 (1)	24/1497 (2)	
Emergency department	30/1513 (2)	8/1497 (1)	

ICU入院率はSystematic Strategyで有意に多かった

Characteristics of the triage process

eTable 3. Characteristics of the Triage Process (Continued)*

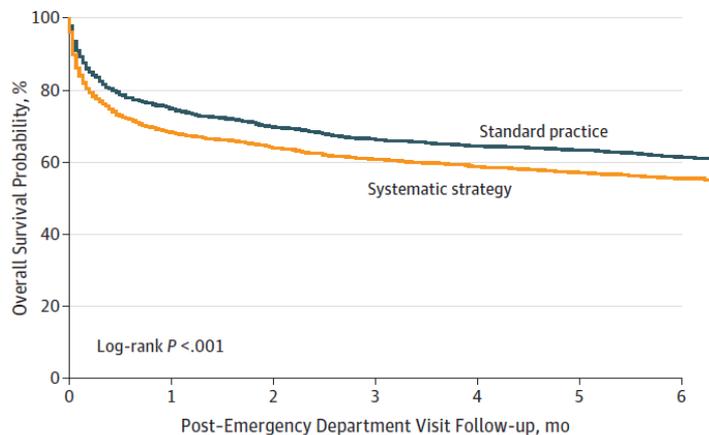
	Systematic strategy (N=1,518)	Standard strategy (N=1,518)	P Value
ED physicians: opinion about ICU admission - no./no. total (%)			
Favorable	1,327/1,513 (88)	875/1,425 (61)	<0.001
Unfavorable	186/1,513 (12)	550/1,425 (39)	
ED physicians: reason for not proposing ICU admission- no./no. total (%)			
Patient is too well	66/179 (37)	209/390 (54)	0.001
No expected benefit due to underlying disease	69/179 (39)	113/390 (29)	
Patient is too sick	44/179 (25)	68/390 (17)	
ICU physicians: opinion about ICU admission - no./no. total (%)			
Favorable	1,110/1,473 (75)	623/938 (66)	<0.001
Unfavorable	363/1,473 (25)	315/938 (34)	
ICU physicians: reason for not proposing ICU admission- no./no. total (%)			
Patient is too well	148/355 (42)	105/292 (36)	0.25
No expected benefit due to underlying disease	115/355 (32)	116/292 (40)	
Patient is too sick	49/355 (14)	40/292 (14)	
Few available beds	43/355 (12)	31/292 (11)	

Systematic strategy
の群の方が救急医も
集中治療医も
ICU入院を推奨

Primary outcome

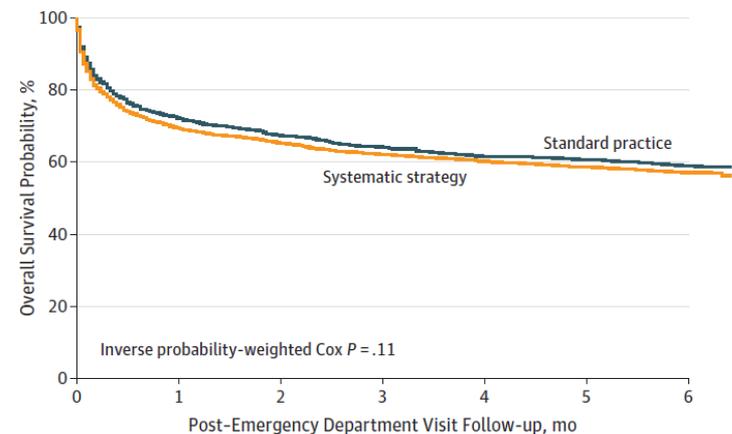
Outcomes	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	Difference in Mean or Rate (95% CI)	Relative Risk (95% CI)	Absolute Risk Difference, % (95% CI) ^a	P Value ^b
Death at 6 mo (primary outcome), No. (%)	685 (45)	588 (39)	6 (3 to 10)	1.16 (1.07 to 1.26)	-6 (-9 to -3)	<.001
Adjusted analysis ^c				1.05 (0.96 to 1.14)	-2 (-6 to 2)	.28

A Unadjusted survival probability



No. at risk	0	1	2	3	4	5	6
Standard practice	1518	1126	1042	992	961	941	912
Systematic strategy	1518	1029	966	919	887	860	826

B Inverse probability-weighted adjusted survival probability



No. at risk	0	1	2	3	4	5	6
Standard practice	1518	1126	1042	992	961	941	912
Systematic strategy	1518	1029	966	919	887	860	826

6か月後の死亡率はsystematic strategyで有意に多かった
Baseline characteristicsで補正後は死亡率に有意差はなかった

Secondary outcome

Outcomes	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	Difference in Mean or Rate (95% CI)	Relative Risk (95% CI)	Absolute Risk Difference, % (95% CI) ^a	P Value ^b
Death at 6 mo (primary outcome), No. (%)	685 (45)	588 (39)	6 (3 to 10)	1.16 (1.07 to 1.26)	-6 (-9 to -3)	<.001
Adjusted analysis ^c				1.05 (0.96 to 1.14)	-2 (-6 to 2)	.28
Intensive care unit admission rate, No. (%)	932 (61)	516 (34)	27 (24 to 31)	1.80 (1.66 to 1.95)	-27 (-31 to -24)	<.001
Adjusted analysis ^c				1.68 (1.54 to 1.82)	-24 (-28 to -21)	<.001
In-hospital mortality, No. (%)	451 (30)	326 (21)	9 (5 to 11)	1.39 (1.23 to 1.57)	-9 (-12 to -5)	<.001
Adjusted analysis ^c				1.18 (1.03 to 1.33)	-4 (-8 to -1)	.03
Decrease in score in ≥ 1 domain of Index of Independence in ADLs, No./total No. (%) ^d	463/680 (68)	394/657 (60)	8 (3 to 13)	1.06 (0.99 to 1.13)	-4 (-8 to 0)	.08
Adjusted analysis ^c				1.02 (0.99 to 1.05)	-2 (-3 to 0)	.10
SF-12 physical component score at 6 mo, mean (95% CI) ^e	36.7 (35.9-37.5)	36.2 (35.5-37.0)	0.5 (-0.6 to 1.5)	0.95 (-0.16 to 2.07) ^f		.09
Adjusted analysis ^c				0.56 (-0.39 to 1.53) ^f		.24
SF-12 mental component score at 6 mo, mean (95% CI) ^e	44.6 (44.1-45.1)	43.7 (43.2-44.2)	0.9 (0.1 to 1.6)	1.05 (0.21 to 1.90) ^f		.02
Adjusted analysis ^c				0.98 (0.15 to 1.81) ^f		.02

ICU入院はSystematic Strategyで有意に多かった
Baseline characteristics補正後も有意に多かった

Secondary outcome

Outcomes	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	Difference in Mean or Rate (95% CI)	Relative Risk (95% CI)	Absolute Risk Difference, % (95% CI) ^a	P Value ^b
Death at 6 mo (primary outcome), No. (%)	685 (45)	588 (39)	6 (3 to 10)	1.16 (1.07 to 1.26)	-6 (-9 to -3)	<.001
Adjusted analysis ^c				1.05 (0.96 to 1.14)	-2 (-6 to 2)	.28
Intensive care unit admission rate, No. (%)	932 (61)	516 (34)	27 (24 to 31)	1.80 (1.66 to 1.95)	-27 (-31 to -24)	<.001
Adjusted analysis ^c				1.68 (1.54 to 1.82)	-24 (-28 to -21)	<.001
In-hospital mortality, No. (%)	451 (30)	326 (21)	9 (5 to 11)	1.39 (1.23 to 1.57)	-9 (-12 to -5)	<.001
Adjusted analysis ^c				1.18 (1.03 to 1.33)	-4 (-8 to -1)	.03
Decrease in score in ≥ 1 domain of Index of Independence in ADLs, No./total No. (%) ^d	463/680 (68)	394/657 (60)	8 (3 to 13)	1.06 (0.99 to 1.13)	-4 (-8 to 0)	.08
Adjusted analysis ^c				1.02 (0.99 to 1.05)	-2 (-3 to 0)	.10
SF-12 physical component score at 6 mo, mean (95% CI) ^e	36.7 (35.9-37.5)	36.2 (35.5-37.0)	0.5 (-0.6 to 1.5)	0.95 (-0.16 to 2.07) ^f		.09
Adjusted analysis ^c				0.56 (-0.39 to 1.53) ^f		.24
SF-12 mental component score at 6 mo, mean (95% CI) ^e	44.6 (44.1-45.1)	43.7 (43.2-44.2)	0.9 (0.1 to 1.6)	1.05 (0.21 to 1.90) ^f		.02
Adjusted analysis ^c				0.98 (0.15 to 1.81) ^f		.02

病院内での死亡率はSystematic Strategyで有意に高かった
Baseline characteristics補正後も有意に高かった

Secondary outcome

Outcomes	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	Difference in Mean or Rate (95% CI)	Relative Risk (95% CI)	Absolute Risk Difference, % (95% CI) ^a	P Value ^b
Death at 6 mo (primary outcome), No. (%)	685 (45)	588 (39)	6 (3 to 10)	1.16 (1.07 to 1.26)	-6 (-9 to -3)	<.001
Adjusted analysis ^c				1.05 (0.96 to 1.14)	-2 (-6 to 2)	.28
Intensive care unit admission rate, No. (%)	932 (61)	516 (34)	27 (24 to 31)	1.80 (1.66 to 1.95)	-27 (-31 to -24)	<.001
Adjusted analysis ^c				1.68 (1.54 to 1.82)	-24 (-28 to -21)	<.001
In-hospital mortality, No. (%)	451 (30)	326 (21)	9 (5 to 11)	1.39 (1.23 to 1.57)	-9 (-12 to -5)	<.001
Adjusted analysis ^c				1.18 (1.03 to 1.33)	-4 (-8 to -1)	.03
Decrease in score in ≥1 domain of Index of Independence in ADLs, No./total No. (%) ^d	463/680 (68)	394/657 (60)	8 (3 to 13)	1.06 (0.99 to 1.13)	-4 (-8 to 0)	.08
Adjusted analysis ^c				1.02 (0.99 to 1.05)	-2 (-3 to 0)	.10
SF-12 physical component score at 6 mo, mean (95% CI) ^e	36.7 (35.9-37.5)	36.2 (35.5-37.0)	0.5 (-0.6 to 1.5)	0.95 (-0.16 to 2.07) ^f		.09
Adjusted analysis ^c				0.56 (-0.39 to 1.53) ^f		.24
SF-12 mental component score at 6 mo, mean (95% CI) ^e	44.6 (44.1-45.1)	43.7 (43.2-44.2)	0.9 (0.1 to 1.6)	1.05 (0.21 to 1.90) ^f		.02
Adjusted analysis ^c				0.98 (0.15 to 1.81) ^f		.02

ADLが1以上低下した割合は両群間で有意差を認めなかった
Baseline characteristics補正後も有意差を認めなかった

Secondary outcome

baselineのindex of ADL

Index of ADL	Systematic strategy (N=1,330)	Standard strategy (N=1,200)
< 4.0	5 (0.4)	16 (1)
4.0	109 (8)	106 (9)
4.5	106 (8)	63 (5)
5.0	134 (10)	103 (9)
5.5	140 (11)	121 (10)
6.0	836 (63)	791 (66)

6か月後のindex of ADL

Index of ADL**	Systematic strategy (N=750)	Standard strategy (N=778)	P Value
0.0	18 (2)	21 (3)	0.09
0.5	25 (3)	17 (2)	
1.0	25 (3)	34 (4)	
1.5	15 (2)	5 (1)	
2.0	24 (3)	27 (3)	
2.5	27 (4)	20 (3)	
3.0	31 (4)	28 (4)	
3.5	45 (6)	36 (5)	
4.0	47 (6)	40 (5)	
4.5	55 (7)	52 (7)	
5.0	77 (10)	98 (13)	
5.5	139 (19)	126 (16)	
6.0	222 (30)	274 (35)	

どちらの群もADLはbaselineより著しく低下している

Secondary outcome

Outcomes	Systematic Strategy (n = 1518)	Standard Practice (n = 1518)	Difference in Mean or Rate (95% CI)	Relative Risk (95% CI)	Absolute Risk Difference, % (95% CI) ^a	P Value ^b
Death at 6 mo (primary outcome), No. (%)	685 (45)	588 (39)	6 (3 to 10)	1.16 (1.07 to 1.26)	-6 (-9 to -3)	<.001
Adjusted analysis ^c				1.05 (0.96 to 1.14)	-2 (-6 to 2)	.28
Intensive care unit admission rate, No. (%)	932 (61)	516 (34)	27 (24 to 31)	1.80 (1.66 to 1.95)	-27 (-31 to -24)	<.001
Adjusted analysis ^c				1.68 (1.54 to 1.82)	-24 (-28 to -21)	<.001
In-hospital mortality, No. (%)	451 (30)	326 (21)	9 (5 to 11)	1.39 (1.23 to 1.57)	-9 (-12 to -5)	<.001
Adjusted analysis ^c				1.18 (1.03 to 1.33)	-4 (-8 to -1)	.03
Decrease in score in ≥ 1 domain of Index of Independence in ADLs, No./total No. (%) ^d	463/680 (68)	394/657 (60)	8 (3 to 13)	1.06 (0.99 to 1.13)	-4 (-8 to 0)	.08
Adjusted analysis ^c				1.02 (0.99 to 1.05)	-2 (-3 to 0)	.10
SF-12 physical component score at 6 mo, mean (95% CI) ^e	36.7 (35.9-37.5)	36.2 (35.5-37.0)	0.5 (-0.6 to 1.5)	0.95 (-0.16 to 2.07) ^f		.09
Adjusted analysis ^c				0.56 (-0.39 to 1.53) ^f		.24
SF-12 mental component score at 6 mo, mean (95% CI) ^e	44.6 (44.1-45.1)	43.7 (43.2-44.2)	0.9 (0.1 to 1.6)	1.05 (0.21 to 1.90) ^f		.02
Adjusted analysis ^c				0.98 (0.15 to 1.81) ^f		.02

身体的なQOLには有意差はなかったが、
精神面でのQOLはSystematic Strategyで有意に良かった
Baseline characteristics補正後も同様の結果

Discussion

結果の解釈

本研究では介入群でICU入院率と6か月死亡率が高かったが、補正後は特に有意差は出ず、他のoutcomeについても有意差は出なかった。

介入群の死亡率が高かったのは、早期の治療撤退が多く、それが高い死亡率につながった可能性がある。ICU滞在期間は両群ともに差はなかった。

今回ICU CUB1 studyから推測した予後の良い群を選んだため、死亡率が高率な患者を除いて施行できた有意義なstudyである。

また死亡率だけでなく、QOLやADLについてもfollowできた。

limitation

- standard practiceの方が募集期間が長く、高齢者医療について、世俗の風潮が変わった影響がでた可能性
- 介入の性質上、groupの割り付けは盲検化していない
- 延命治療の治療撤退についてのデータがない
- systematic strategy ではより重症患者がICU入院となった
- ICU入院で予後が良い患者は、一般症でもケアできた
- ICU入院を取り下げた理由について評価していない
- それぞれの施設で医療ケアの質の違いがあった
- もともとICU入院が少ない施設は一般症での管理が良い

結論

医療資源の分配や支出の調整を考えたとき、高齢者のICU入院は長期的効果がないことを考慮すると、重症な高齢者をICUに入院させることは好まれないだろう。

しかし本研究は高齢者のICU入院を推奨しないものではない。高齢者もベースの健康状態や予備力あそれぞれであり、ICU入院の適応があるかは systematically & thoughtfully に決めるべきである。

私見

ICU CUB1 studyによると……

そもそも医者はICU入院の適応を考えると、状態が良すぎるor状態が悪すぎると判断して、ICU入院の適応から外していた。

→つまり今回の介入で増えたICU入院の患者層は状態の良すぎる人or状態の悪すぎる人たち

→今回の結果によると、そのような人はICU入院を推奨しても、恩恵を受けにくいということ (ICU入院は、予後改善に影響しない)

私見

考えなしのsystematicなICU入院は予後を特別改善させることはなさそう

→ systematically & thoughtfullyが望ましいということは、やはり医者がそれぞれ総合的にICU入院を判断する(という従来の)方法で良いのだろうか

私見

もしくはcriteriaの設定がまだ不十分な可能性はあり

実際ICU CUB1 studyのcriteriaは半分近くがあいまいなcriteriaとなっている

さらなるstudyをもとに、より適した高齢者のICU入院に関するcriteriaを作成していくことが必要