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JAMA | Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit

The Oxygen-ICU Randomized Clinical Trial

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Design

- RCT (randomized controlled trial)
  - computerized random-number generator 1:1 ratio.

- Single center (medical-surgical ICU, Modena University Hospital, Italy)

Studiedeltagare

Inklusionskriterier:

- Alla > 18 år med förväntad IVA vård > 72 timmar
- mars 2010 till oktober 2012

Exklusionskriterier:

- Gravida, återinläggning, beh begr, immunsupprimerade, neutropena, akut på kronisk lungsvikt, måttlig-svår ARDS

Exponering

Protokoll gruppen:

- Lägsta möjliga FiO2 för att hålla pO2 70-100 mm Hg (9.3-13.3 kPa) alt SpO2 94-98%

Kontroll gruppen:

- FiO2 minst 0,4 för att hålla pO2 upp till 150 mm Hg (20 kPa) och SpO2 97-100%. FiO2 1.0 vid intubation, sugning och transport

Minst en blodgaskontroll per dag

Utfall

Primär outcome:

- IVA mortalitet

Sekundära outcome:

- Ny organsvikt (respiratorisk, kardiovaskulär, lever, njure)
- Behov av reop hos kirurgpat
- Infektion (i blod, luftväg eller opsår)
- Hosp mortalitet och ventilator-fria timmar på IVA – ej predefinerade sekundära outcomes

Power

Planerad sample size 660 pat under 2 år för att hitta en absolut mortalitetsskillnad på 6%

Baserat på IVA mortalitet på 23%, signifikansnivå 5% och power 80%

Studien bröts efter 480 patienter


VIGILI DEL FUOCO

Figure 1. Patient Flow Diagram of the Oxygen-ICU Trial

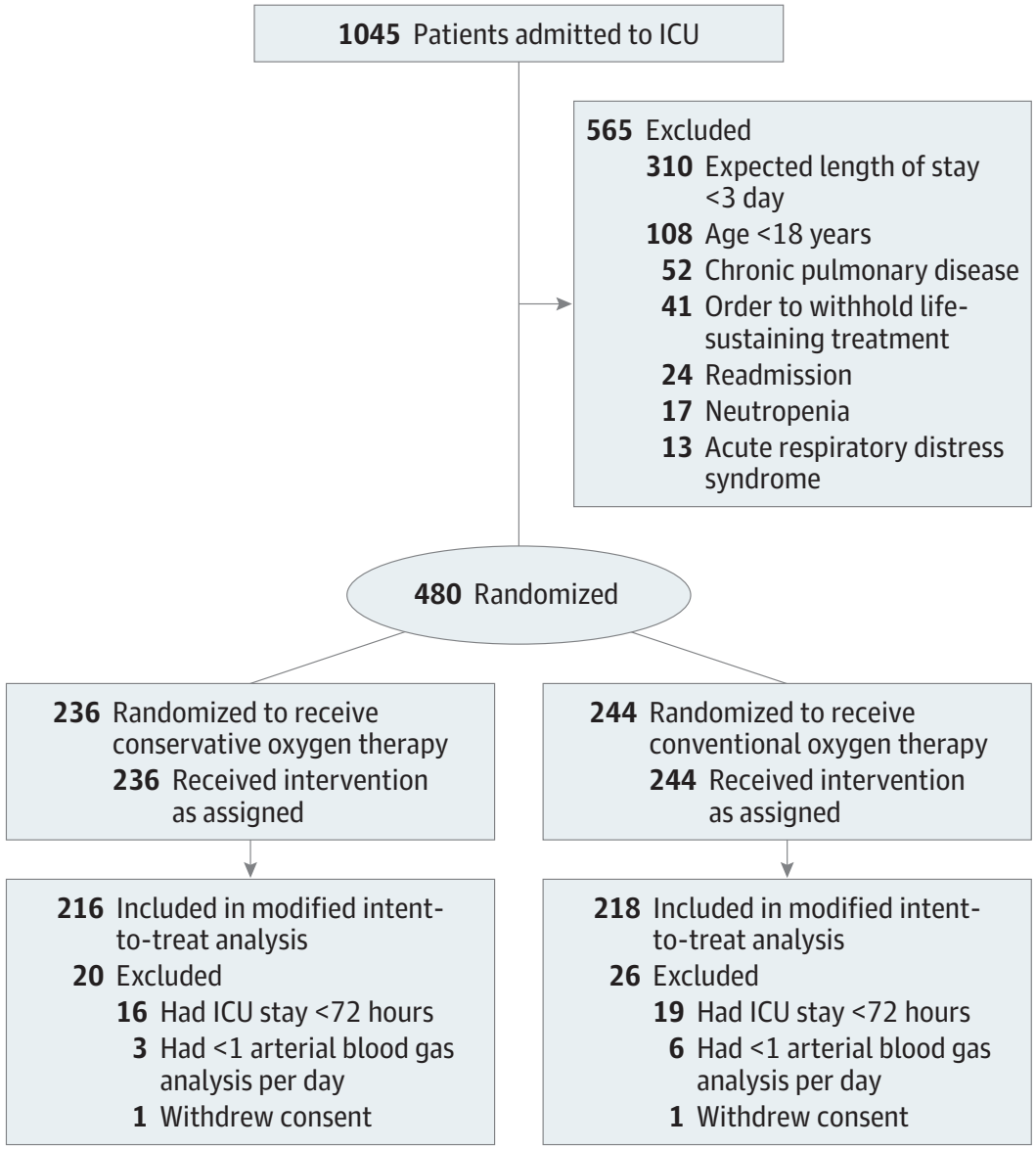


Table 1. Characteristics of the Patients at Study Inclusion by Oxygen Therapy Group

	Oxygen Therapy Group, No. (%)	
	Conservative (n = 216)	Conventional (n = 218)
Sex, female	95 (44.0)	93 (42.7)
Age, median (IQR), y	63 (51-74)	65 (52-76)
Type of ICU admission		
Medical	77 (35.7)	86 (39.5)
Surgical	139 (64.3)	132 (60.7)
Preexisting condition		
Chronic obstructive pulmonary disease	7 (3.2)	11 (5.0)
Chronic renal failure	13 (6.0)	13 (6.0)
Chronic liver disease	28 (12.9)	31 (14.2)
Cancer	72 (33.3)	70 (31.1)
Respiratory failure	121 (56.0)	129 (59.2)
Mechanical ventilation	143 (66.2)	148 (67.9)
Shock	68 (31.4)	72 (33.0)
Septic	46 (21.3)	47 (21.6)
Hypovolemic or hemorrhagic	7 (3.2)	9 (4.1)
Cardiogenic	12 (5.6)	8 (3.7)
Mixed	3 (1.4)	8 (3.7)
Liver failure	40 (18.5)	45 (20.6)
Renal failure	32 (14.8)	35 (16.1)
Documented infections[a]	81 (37.5)	88 (40.4)
SAPS II, median (IQR) score[a]	37 (26-49)	39 (28-55)

eTable 1. *Post-hoc* analysis of ICU mortality in patients sub-grouped by patient characteristics at study enrolment and their ICU length of stay

	Conservative O2 therapy N = 216	**ConventionalO2 therapy N = 218**	**Absolute risk reduction (95% CI)**	**P value**
SAPS, no. (%)*				
≤ 38	3/117 (2.6)	6/104 (5.8)	3.2 (-2.4 – 9.7)	0.23
>38	22/99 (22.2)	38/114 (33.3)	11-1 (-1.0 – 22.6)	0.072
Type of ICU admission, no. (%)				
medical	18/77 (23.4)	30/86 (34.9)	11.5 (-2.5 – 24.8)	0.086
surgical	7/139 (5.0)	14/132 (10.6)	5.6 (-0.9 – 12.5)	0.086
Respiratory failure at admission, no. (%)	21/121 (17.4)	39/129 (30.2)	12.8 (2.3 – 23.0)	0.017
Mechanical Ventilation at admission, no. (%)	23/143 (16.1)	40/148 (27.0)	10.9 (1.5 – 20.2)	0.023
Shock at admission, no. (%)	20/68 (29.4)	27/72 (37.5)	8.1 (-7.5 – 23.0)	0.31
Liver failure at admission, no. (%)	9/40 (22.5)	15/45 (33.3)	10.8 (-8.4 – 28.6)	0.266
Renal failure at admission, no. (%)	8/32 (25.0)	16/35 (45.7)	20.7 (-2.2 – 40.6)	0.077
Documented infections at admission, no. (%)	22/81 (27.2)	26/88 (29.5)	2.3 (-11.2 – 15.7)	0.73
ICU length of stay, no. (%) *				
≤ 6 days	5/120 (4.2)	15/110 (13.6)	9.4 (2.2– 14.2)	0.011
> 6 days	20/96 (20.8)	29/108 (26.9)	6.1 (-5.8 – 17.4)	0.314

Simplified Acute Physiology Score (SAPS) II ; * Thirty-eight is the overall median value of SAPS II; Six days was the overall median for ICU length of stay

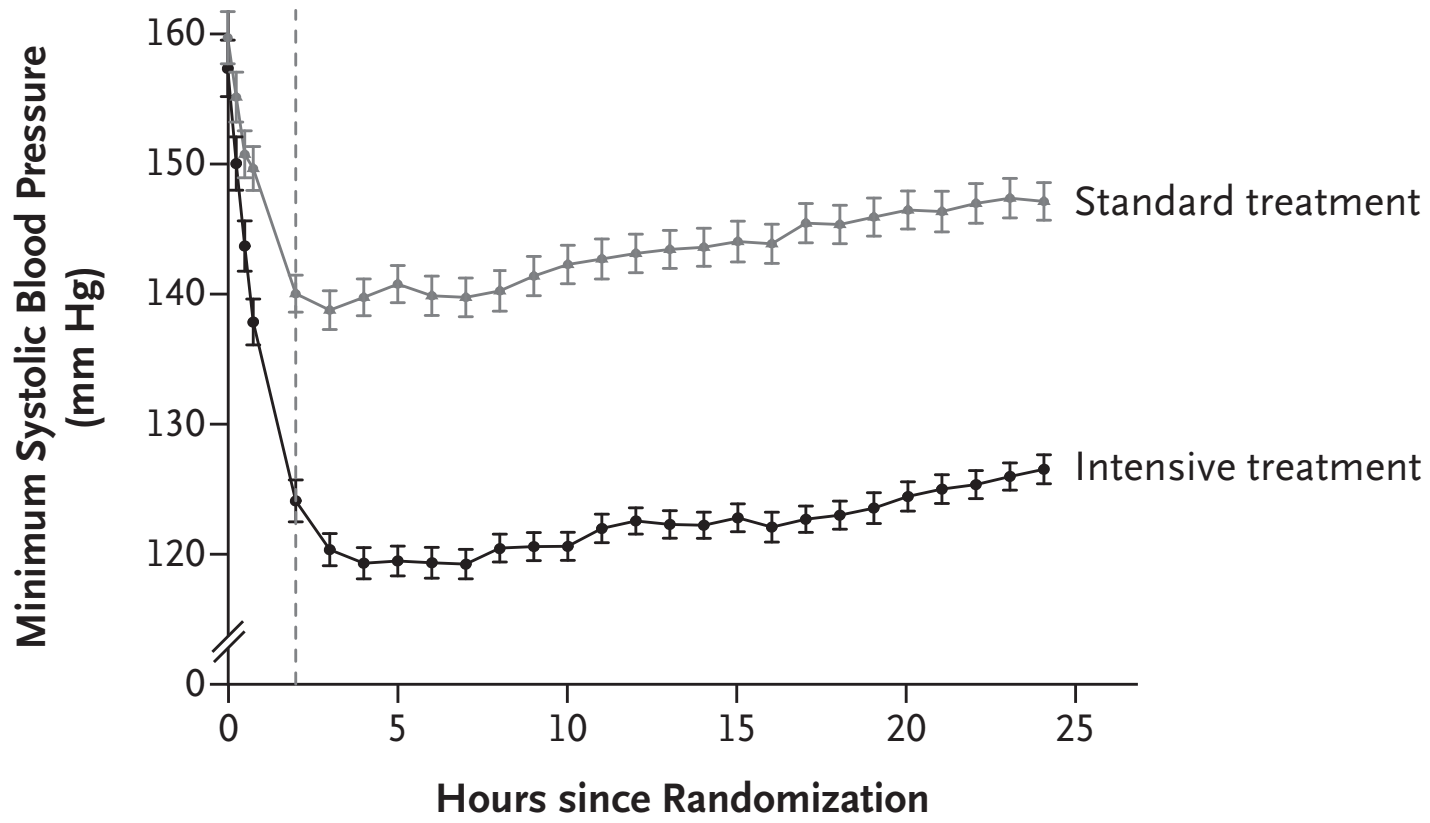
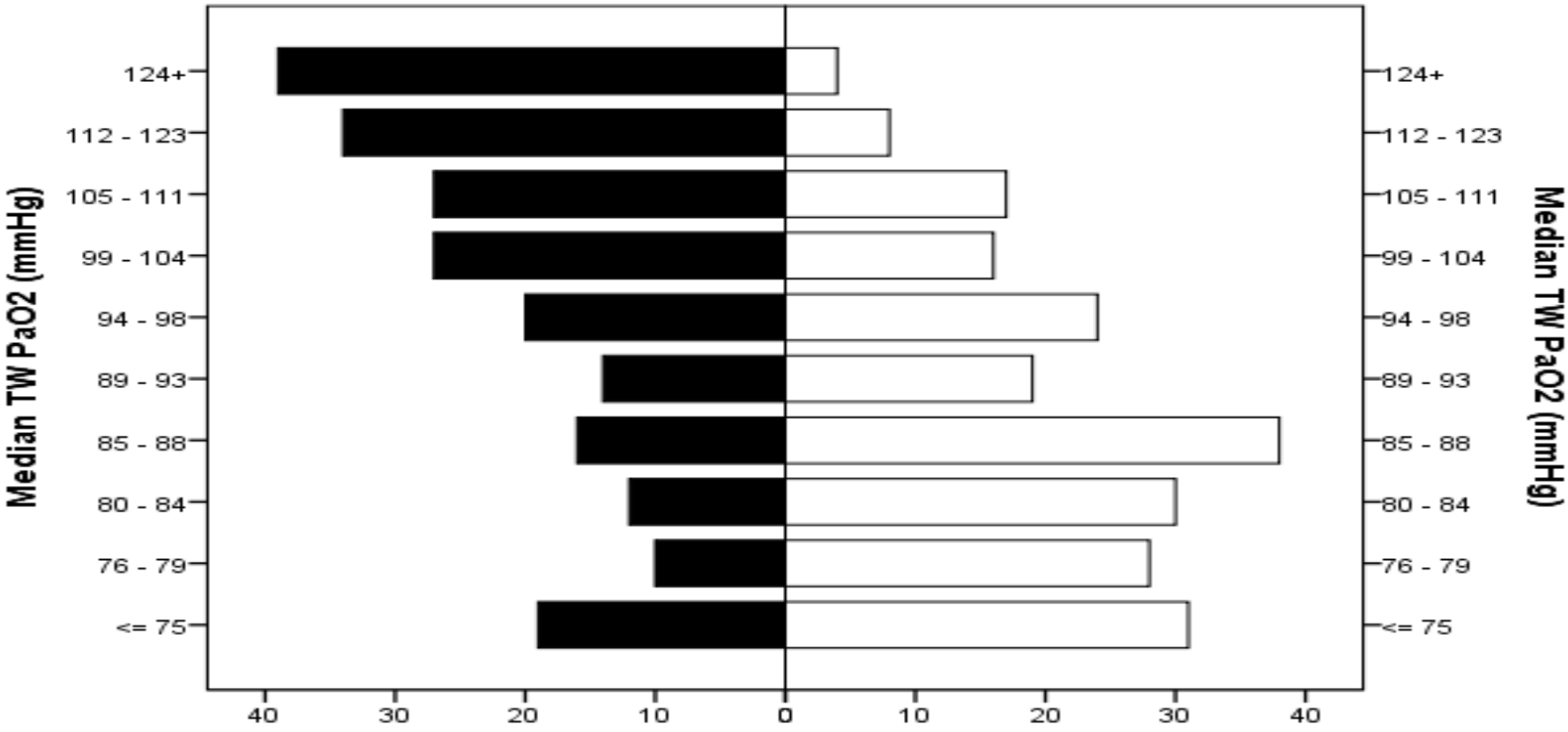


Figure 1. Mean Hourly Minimum Systolic Blood Pressure during the First 24 Hours after Randomization, According to Treatment Group.

The dashed vertical line indicates 2 hours, and I bars 95% confidence intervals.

Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, et al. Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage. N Engl J Med. 2016;375(11):1033-43.



Conventional group (number of patients)

Conservative group (number of patients)

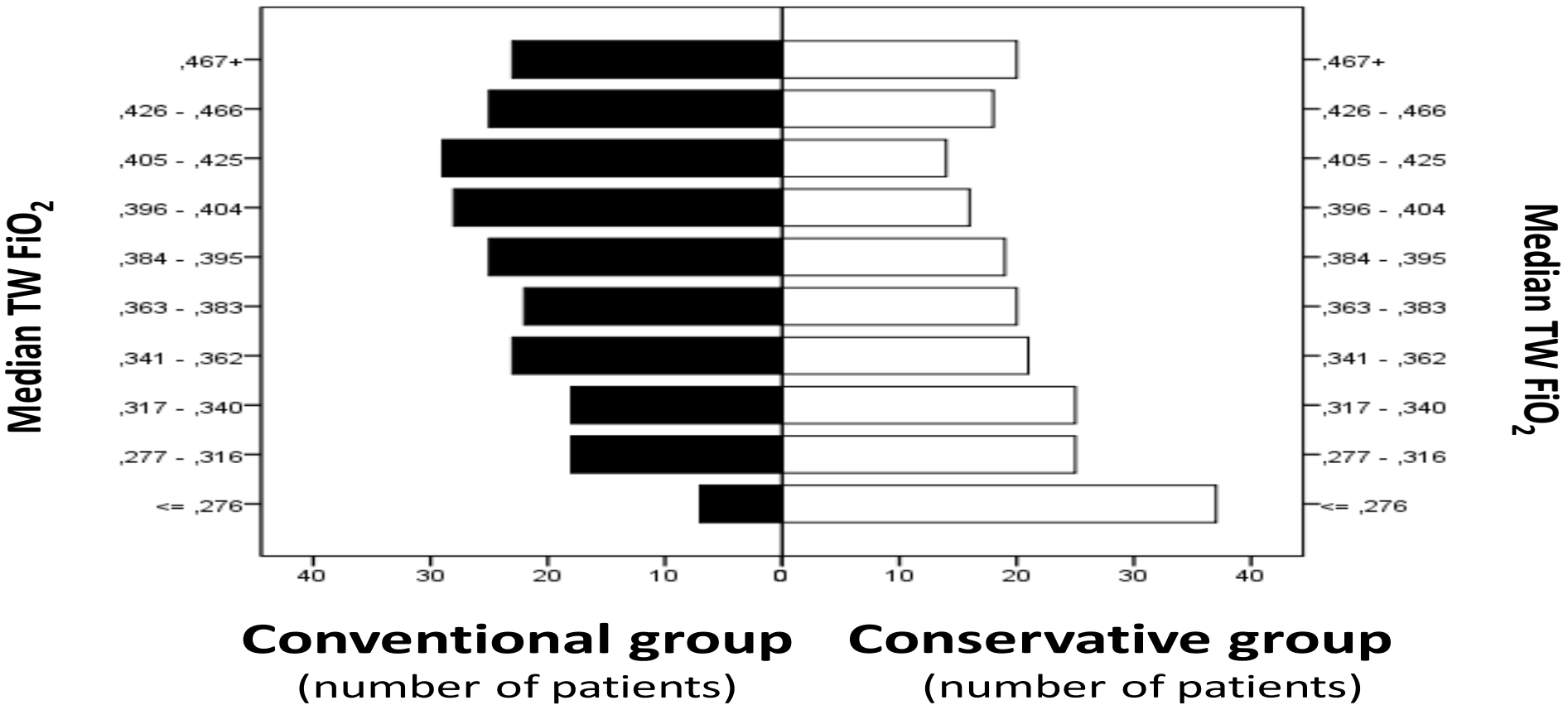
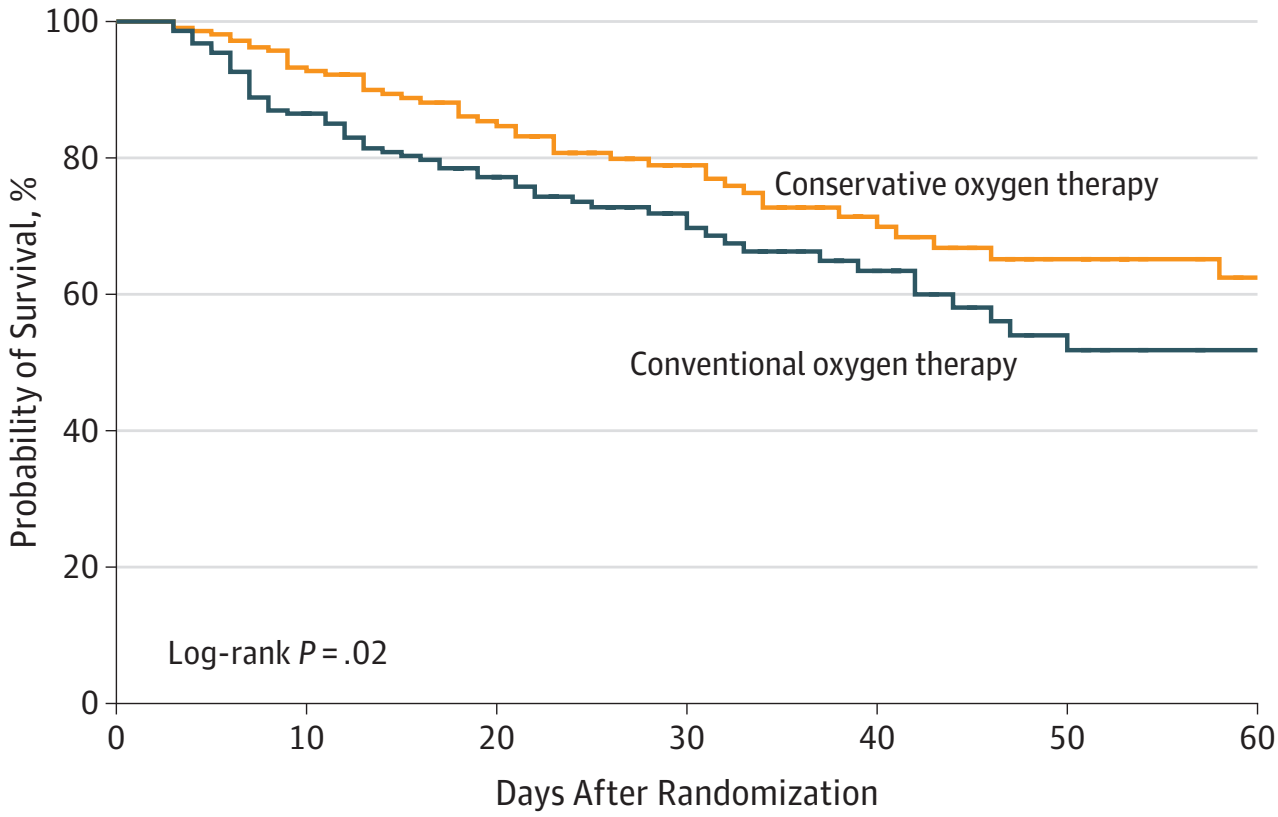

Median TW FiO2
,467+
,426 - ,466
,405 - ,425
,396 - ,404
,384 - ,395
,363 - ,383
,341 - ,362
,317 - ,340
,277 - ,316
<= ,276
40
30
20
10
0
10
20
30
40
Median TW FiO2
Conventional group
(number of patients)
Conservative group
(number of patients)

Table 2. Primary and Secondary Outcomes

	Oxygen Therapy, No. (%)			
	Conservative (n = 216)	Conventional (n = 218)	Absolute Risk Difference (95% CI)	*P* Value
Primary outcome				
ICU mortality	25 (11.6)	44 (20.2)	0.086 (0.017 to 0.150)	.01
Secondary outcomes				
Hospital mortality	52 (24.2)	74 (33.9)	0.099 (0.013 to 0.182)	.03
New organ failure during ICU stay	41 (19.0)	56 (25.7)	0.067 (−0.012 to 0.145)	.09
Respiratory failure	14 (6.5)	14 (6.4)	−0.126 (−0.189 to −0.064)	.98
Shock	8 (3.7)	23 (10.6)	0.068 (0.020 to 0.120)	.006
Liver failure	4 (1.9)	14 (6.4)	0.046 (0.008 to 0.088)	.02
Renal failure	26 (12.0)	21 (9.6)	−0.024 (−0.084 to 0.035)	.42
New infections during ICU stay	39 (18.1)	50 (22.9)	0.049 (−0.027 to 0.124)	.21
Respiratory	30 (13.9)	37 (17.0)	0.031 (−0.038 to 0.099)	.37
Bacteremia	11 (5.1)	22 (10.1)	0.050 (0.000 to 0.090)	.049
Surgical site[a]	10 (7.2)	12 (9.1)	0.019 (−0.048 to 0.088)	.68
Surgical revision[a]	18 (12.9)	16 (12.1)	−0.008 (−0.088 to 0.073)	.84
Mechanical ventilation–free hours, median (IQR)	72 (35 to 110)	48 (24 to 96)	24 (0 to 46)	.02
ICU length of stay, median (IQR), d	6 (4 to 10)	6 (4 to 11)	0 (0 to 2)	.33
Hospital length of stay, median (IQR), d	21 (13 to 38)	21 (12 to 34)	0 (−5 to 1)	.21

Figure 2. Probability of Survival From Study Inclusion (Day 0) Through Day 60 for Patients in the Conservative and Conventional Oxygen Strategy Groups



No. at risk							
Conservative oxygen therapy	216	201	188	181	173	170	169
Conventional oxygen therapy	218	189	172	163	158	152	152

Analys

Modified Intention to Treat = man exkluderar patienter baserat på events som har hänt efter randomisering.

Intention to Treat = man analyserar alla patienter i gruppen oavsett vad som har hänt.

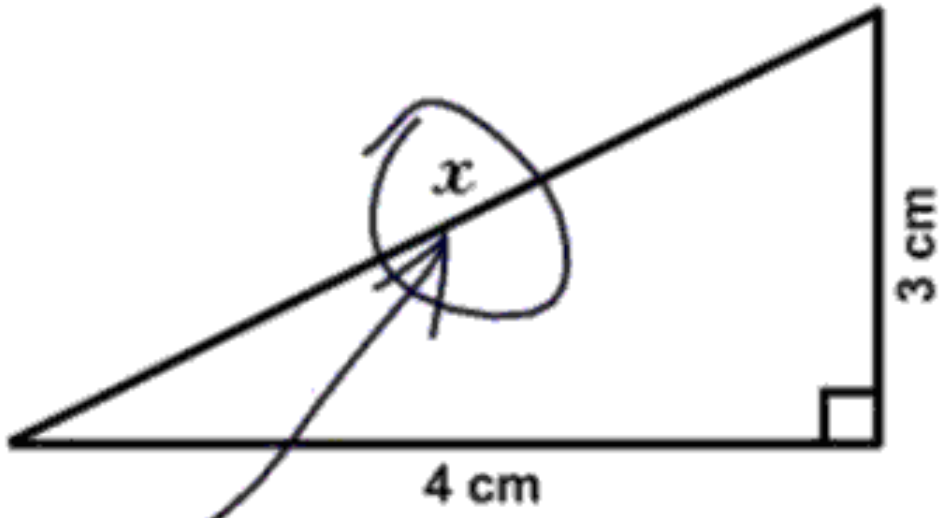
ITT har gjorts och redovisats i supplements

Generaliserbarhet

Single center

IVA mortalitet 23%

Find x.



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