

Supplementary Online Content

Kawazoe Y, Miyamoto K, Morimoto T, et al; Dexmedetomidine for Sepsis in Intensive Care Unit Randomized Evaluation (DESIRE) Trial Investigators. Effect of dexmedetomidine on mortality and ventilator-free days in patients requiring mechanical ventilation with sepsis: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2017.2088

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Sedative and Opioid Usage and Dosing in the First Week

	DEX group	Control group	<i>P</i> value
Day 1 (N=201)			
Fentanyl			
N (%)	76 (76)	79 (78)	.71
Dose, m [IQR], mcg	[16, 390]	240 [25, 460]	.50
Propofol			
N (%)	29 (29)	43 (43)	.04
Dose, m [IQR], mg	0 [0, 40]	0 [0, 200]	.06
Midazolam			
N (%)	21 (21)	40 (40)	.004
Dose, m [IQR], mg	0 [0, 0]	0 [0, 27.5]	.002
Dexmedetomidine			
N (%)	78 (78)	2 (2)	<.001
Dose, m [IQR], mcg	81 [11, 154.5]	0 [0, 0]	<.001
Day 2 (N=197)			
Fentanyl			
N (%)	86 (87)	84 (86)	.81
Dose, m [IQR], mcg	600 [240, 920]	522.5 [290, 720]	.38
Propofol			
N (%)	27(27)	48 (49)	.002
Dose, m [IQR], mg	0 [0, 110]	0 [0, 785]	<.001
Midazolam			
N (%)	15 (15)	41 (42)	<.001
Dose, m [IQR], mg	0 [0, 0]	0 [0, 38]	<.001
Dexmedetomidine N			
(%)	94 (95)	2 (2)	<.001
Dose, m [IQR], mcg	304 [136, 480]	0 [0, 0]	<.001
Day 3 (N=174)			
Fentanyl			
N (%)	72 (83)	72 (83)	>.99
Dose, m [IQR], mcg	720[300, 960]	550 [240, 960]	.21
Propofol			
N (%)	22 (25)	36 (41)	.02

Dose, m [IQR], mg	0 [0, 40]	0 [0, 640]	.01
Midazolam			
N (%)	8 (9)	35 (40)	<.001
Dose, m [IQR], mg	0 [0, 0]	0 [0, 29]	<.001
Dexmedetomidine			
N (%)	77 (89)	1 (1)	<.001
Dose, m [IQR], mcg	336 [125, 480]	0 [0, 0]	<.001
Day 4 (N=152)			
Fentanyl			
N (%)	60 (81)	62 (79)	.81
Dose, m [IQR], mcg	600[180, 1024]	515[191, 960]	.53
Propofol			
N (%)	16 (22)	33 (42)	.006
Dose, m [IQR], mg	0 [0, 0]	0 [0, 457.5]	.02
Midazolam			
N (%)	6 (8)	25 (32)	<.001
Dose, m [IQR], mg	0 [0, 0]	0 [0, 18]	<.001
Dexmedetomidine			
N (%)	60 (81)	2 (3)	<.001
Dose, m [IQR], mcg	254 [68, 510]	0 [0, 0]	<.001
Day 5 (N=137)			
Fentanyl			
N (%)	50 (77)	57 (79)	.75
Dose, m [IQR], mcg	550[124, 960]	600[106, 1056]	.67
Propofol			
N (%)	14 (22)	25 (35)	.09
Dose, m [IQR], mg	0 [0, 0]	0 [0, 537.5]	.10
Midazolam			
N (%)	8 (12)	21 (29)	.02
Dose, m [IQR], mg	0 [0, 0]	0 [0, 13]	.009
Dexmedetomidine N			
(%)	52 (80)	2 (3)	<.001
Dose, m [IQR], mcg	204 [66, 360]	0 [0, 0]	<.001
Day 6 (N=115)			
Fentanyl			
N (%)	41 (77)	44 (71)	.44

Dose, m [IQR], mcg	569[0,1097.5]	600[90, 960]	.73
Propofol			
N (%)	10 (19)	26 (42)	.008
Dose, m [IQR], mg	0 [0, 0]	0 [0, 597.5]	.01
Midazolam			
N (%)	9 (17)	17 (27)	.18
Dose, m [IQR], mg	0 [0, 0]	0 [0, 17]	.16
Dexmedetomidine N			
(%)	43 (81)	1 (2)	<.001
Dose, m [IQR], mcg	192 [40, 480]	0 [0, 0]	<.001
Day 7 (N=110)			
Fentanyl			
N (%)	42 (79)	40 (70)	.28
Dose, m [IQR], mg	600[180, 1200]	600[0, 1077.5]	.45
Propofol			
N (%)	9 (17)	15 (26)	.24
Dose, m [IQR], mg	0 [0, 0]	0 [0, 225]	.23
Midazolam			
N (%)	6 (11)	17 (30)	.02
Dose, m [IQR], mg	0 [0, 0]	0 [0, 12]	.02
Dexmedetomidine N			
(%)	42 (79)	1 (2)	<.001
Dose, m [IQR], mcg	228 [29, 408.5]	0 [0, 0]	<.001

Number of patients was compared with Chi-squared test or Fisher's exact test, and dose of sedatives was compared with Wilcoxon rank sums test.

Abbreviations: m, median; IQR, interquartile range

eTable 2. Secondary Outcome Measurements

	DEX group	Control group	<i>P</i> value
Ventilator days, median [IQR], day	6 [3, 11]	6 [3, 11]	.64
Hospital stay, median [IQR], day	25.5 [16, 47]	30 [18, 58]	.27
DIC, median [IQR]	2 [1, 5]	[1, 4]	.90
RRT, n (%)	38 (38)	39 (39)	.93
CAM- ICU positive, n (%)	44 (44)	45 (45)	.94
CRP, median [IQR], mg/dL	4.9 [2.1, 11.7]	8.1 [3.3, 13.4]	.03
PCT, median [IQR], ng/mL	0.5 [0.1, 3.6]	0.9 [0.2, 5.5]	.12
Prealbumin, median [IQR], mg/dL	11.1 [6.8, 16.7]	9.6 [7.3, 13.9]	.27
Energy intake by EN, median [IQR], kcal	4.5 [0, 600]	0 [0, 400]	.11
Urinary output, median [IQR], mL	1152.5 [336, 2074]	1026.5 [66, 1653]	.06
eGFR, median [IQR], mL/min/1.73m ²	58.1 [26.9, 92.8]	55.1 [22.2, 87.6]	0.86 .53
Creatinine, median [IQR], mg/dL	[0.59, 1.92]	0.96 [0.60, 2.20]	23 [15, .53
BUN, median [IQR], mg/dL	43]	28 [15, 43.5]	.95

CRP, PCT, Prealbumin, eGFR, Creatinine and BUN were obtained on 14th days or the last data if discharged earlier from hospital. DIC, RRT, Energy intake and Urinary output were evaluated in the last day of ICU stay. CAM-ICU was evaluated in intensive care unit every day.

Abbreviations: IQR, interquartile range; DIC, Disseminated Intravascular Coagulation; RRT, renal replacement therapy; CAM-ICU, Confusion Assessment Method for intensive care unit; CRP, C-reactive protein; EN, enteral nutrition; PCT, procalcitonin; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen

Sedation & analgesia protocol

Group A

- Dexmedetomidine titrated 0.1~0.7µg/kg/h
- Start Dexmedetomidine 0.1µg/kg/h from the beginning and then titrate as needed
- Dexmedetomidine over 24hs
- fentanyl 0~5µg/kg/h as needed
- minimum propofol/midazolam as needed

- VAS* goal ≤ 2 , (or NRS goal ≤ 3)
(under deep sedation, BPS** ≤ 4)
- CAMICU*** goal : negative
- RASS**** goal : 0(day), -2(night)

Group B

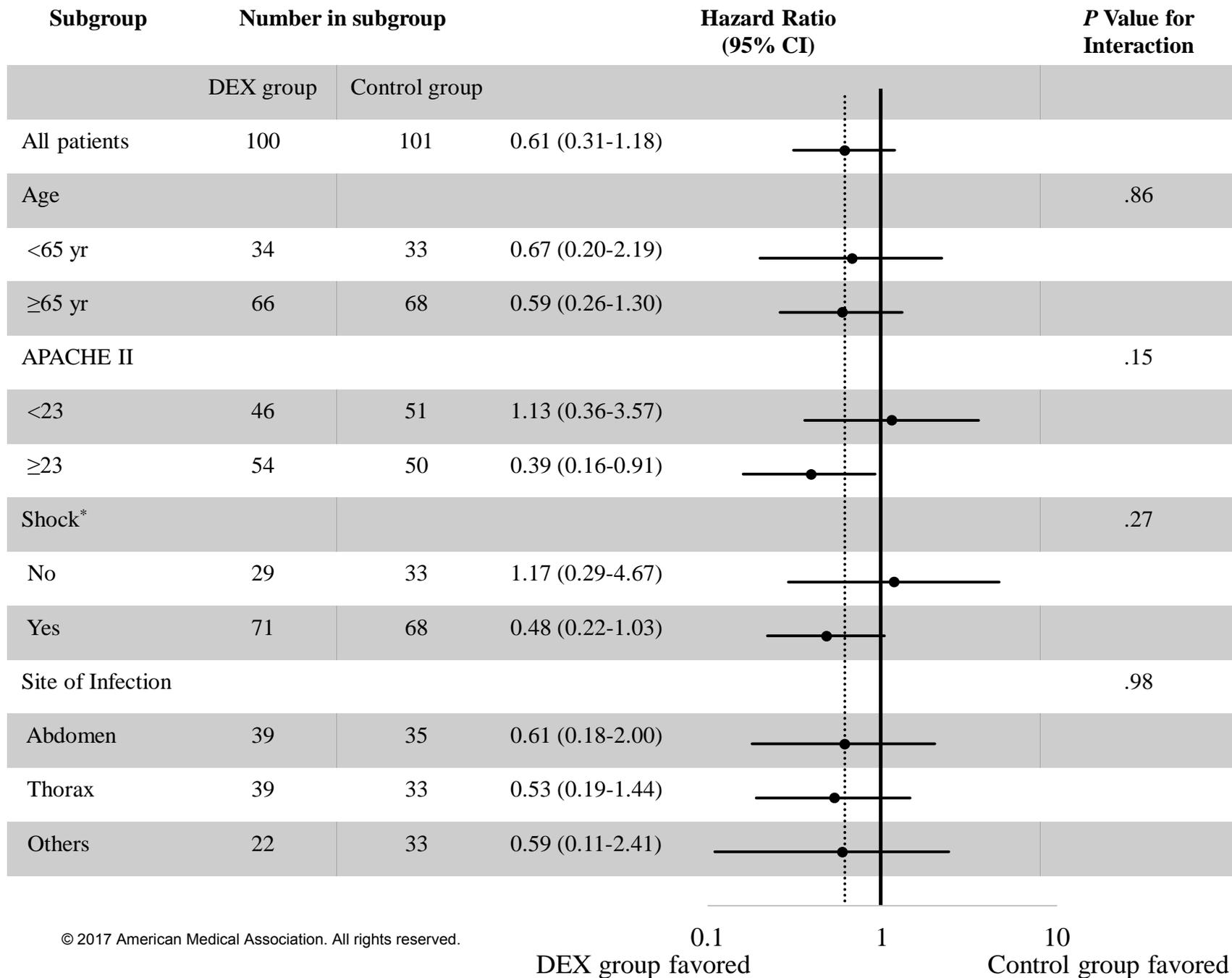
- Conventional propofol- / midazolam-based sedation without Dexmedetomidine
- fentanyl 0~5µg/kg/h as needed
- propofol titrated 0~3mg/kg/h
- midazolam titrated 0~0.15mg/kg/h

- same as group A

*VAS : Visual analogue scale **BPS : Behavioral pain scale

***CAMICU : Confusion assessment method in the ICU

****RASS : Richmond agitation-sedation scale



eFigure 2. Results of Subgroup Analyses on Mortality

* Shock was defined as 3 or more cardiovascular components on the Sequential Organ Failure Assessment.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval.