

The impact of timing of antibiotic administration on clinical outcomes in patients with community-onset severe sepsis and septic shock: a multicentre observational study

YK Yoon¹, KS Yang¹, DW Park¹, BC Chun¹, JW Sohn¹, HJ Cheong¹, JY Choi⁹, HJ Choi², YH Choi³, HY Kim⁴, JS Eom⁵, SI Kim⁶, YG Song⁹, KR Peck⁷, YS Kim⁸, JM Kim⁹, MJ Kim¹

¹Korea University College of Medicine, ²Ewha Woman's University College of Medicine, ³Ajou University Medical College, ⁴Yonsei University Wonju Medical College, ⁵Hanlym University Medical College, ⁶Catholic University Medical College, ⁷Sungkyunkwan University, ⁸Ulsan University Medical College and ⁹Yonsei University Medical College; Seoul, Republic of Korea



BACKGROUND

- ❖ **Early appropriate antibiotic therapy: cornerstone of sepsis care**
 - Timing of antibiotic therapy used as a quality
 - Concern over the antibiotic overuse and misuse
- ❖ **A key for mortality reduction: time-points of antibiotic therapy**

Year	Author	Study	Antibiotics
2001	Rivers <i>et al</i>	Early goal directed therapy	Within 6 hrs
2008	Dellinger <i>et al</i>	Surviving Sepsis Campaign	Within 1 hr
2013	Dellinger <i>et al</i>	Sepsis bundle	Within 3 hrs
2014	Yealy <i>et al</i>	ProCESS	Within 3 hrs
2014	Peake <i>et al</i>	ARISE	Median of 70 min
2015	Mouncey <i>et al</i>	ProMISe	Median of 2.5 hrs

Aims of Study

- ❖ **To evaluate the association between timing of antibiotic administration and mortality in the patients with community-acquired severe sepsis or septic shock**

MATERIALS and METHODS

- **Study design and setting**
 - ❖ Multi-center retrospective study
 - ❖ From 12 teaching hospitals in the Republic of Korea
 - ❖ From May 2005 to December 2008
 - ❖ Using the Korean Sepsis Registry System (KSRS)
- ❖ **Inclusion criteria**
 - ❖ Adult patients (≥18 years)
 - ❖ With community-acquired (CA) severe sepsis or septic shock
 - ❖ Within 24 hours of getting to the emergency room or ICUs
- ❖ **Exclusion criteria**
 - ❖ Nosocomial infections
- ❖ **Statistical analysis**
 - ❖ IBM SPSS Statistics version 20.0 (IBM®, Armonk, NY, USA)
 - ❖ SAS 9.2 (SAS Institute Inc., Cary, NC, USA)

RESULTS

Figure 1. Selection process of study patients

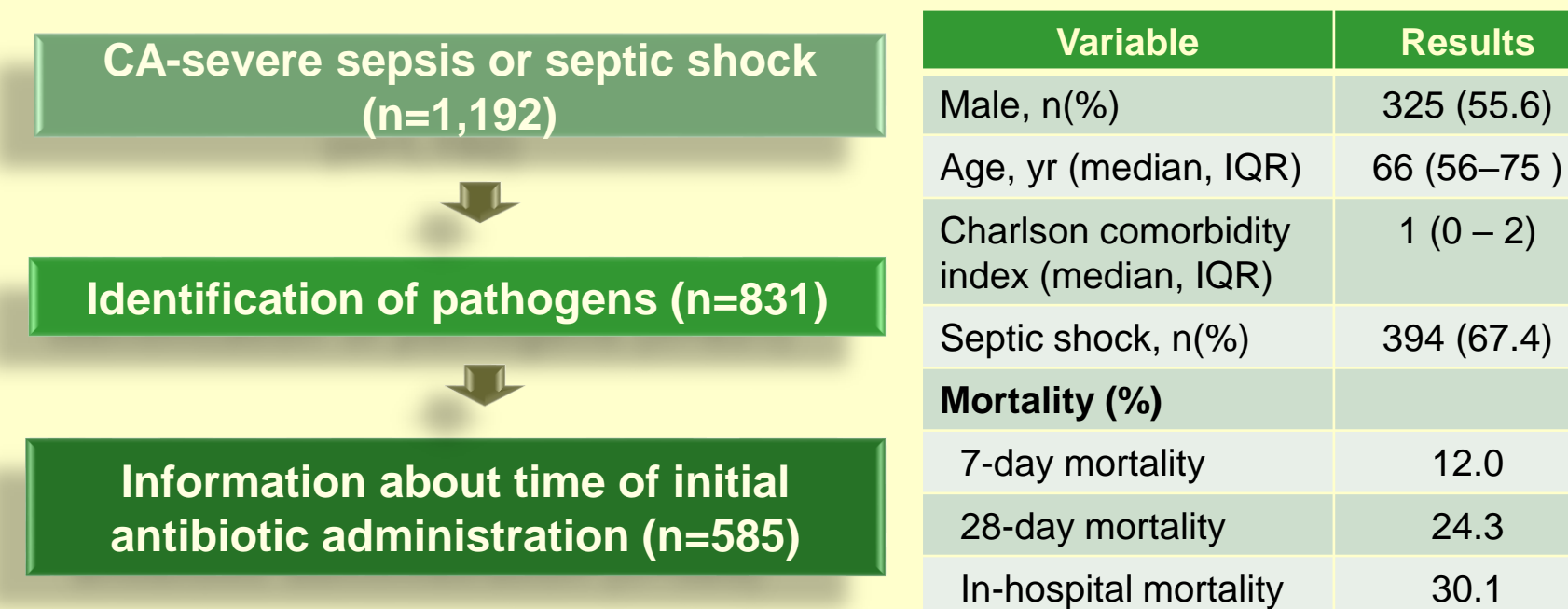


Figure 2. Distribution of primary site of infection

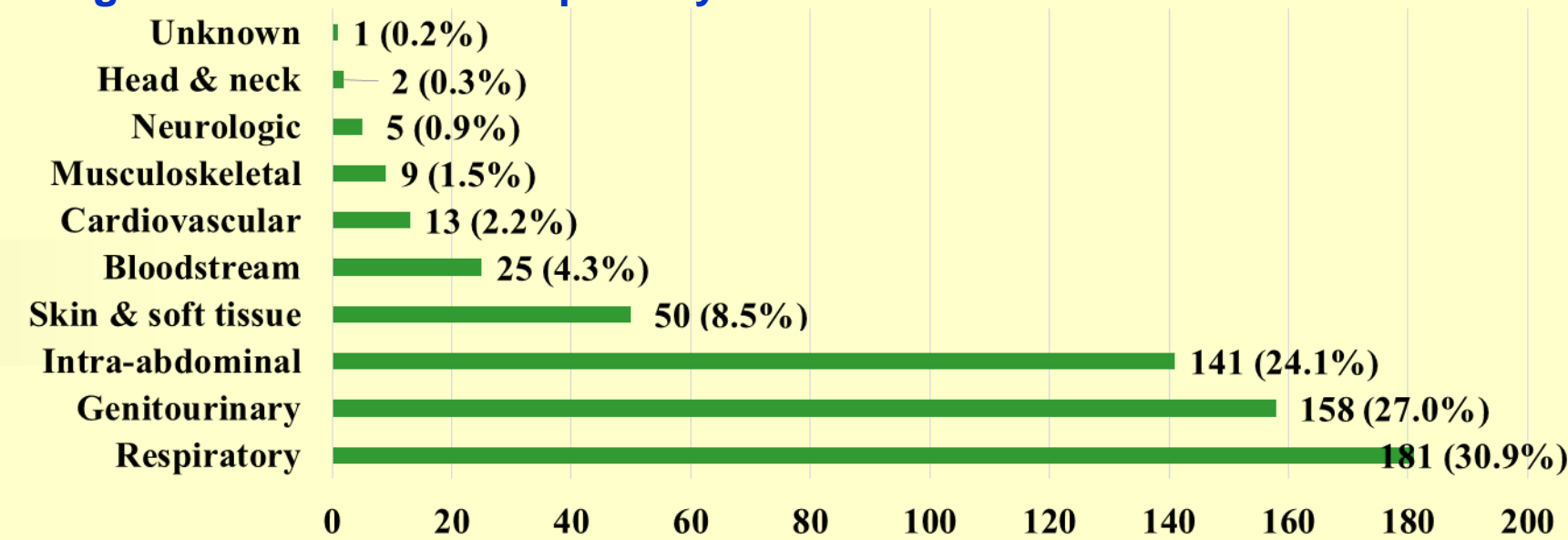


Figure 3. Distribution of timing in hours to the initial antibiotic therapy

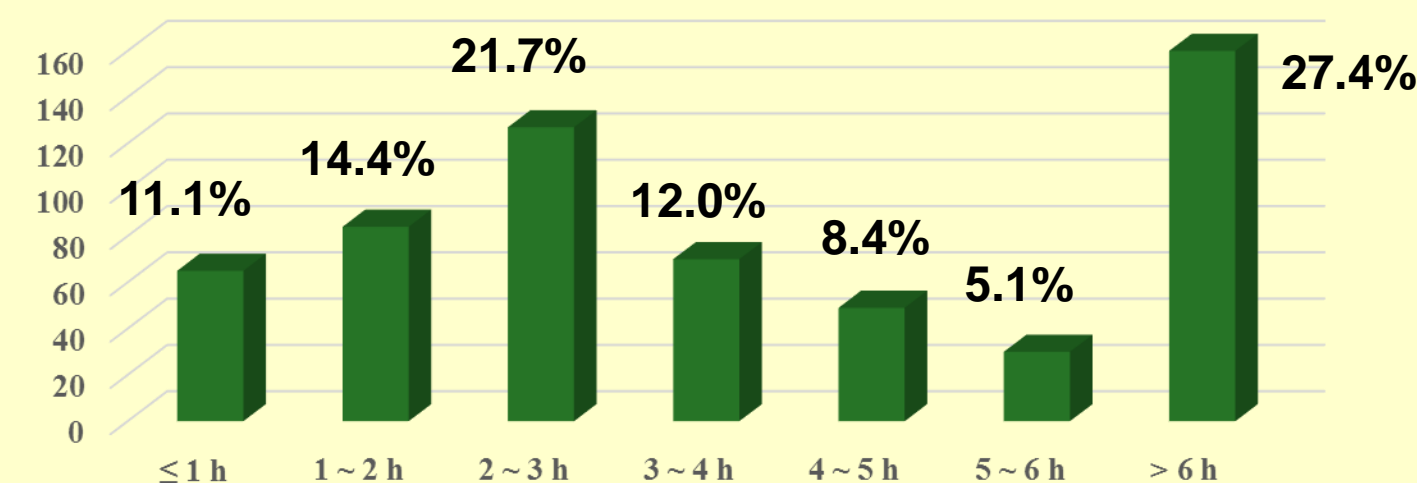


Table 1. Odds ratio and probability of 28-day mortality based on the interval between time to visit the hospital

Time-to antibiotics (hrs)	No. of patients (%)	No. of mortality (%)	OR (95% CI)	P value
≤ 1	65 (11.1)	15 (23.1)	0.93 (0.53-1.64)	0.802
> 1	520 (88.9)	127 (24.4)		
≤ 2	149 (25.5)	35 (23.5)	0.97 (0.64-1.47)	0.869
> 2	436 (74.5)	107 (24.5)		
≤ 3	276 (47.2)	69 (25.0)	1.18 (0.89-1.56)	0.253
> 3	309 (52.8)	73 (23.6)		
≤ 4	346 (59.1)	88 (25.4)	1.19 (0.60-2.36)	0.619
> 4	239 (40.9)	54 (22.6)		
≤ 5	395 (67.5)	101 (25.6)	1.14 (0.57-2.30)	0.713
> 5	190 (32.5)	41 (21.6)		
≤ 6	425 (72.6)	107 (25.2)	0.75 (0.32-1.75)	0.507
> 6	160 (27.4)	35 (21.9)		

Table 2. Odds ratio and probability of 28-day mortality based on the interval between time to visit the hospital

Time to antibiotics (hr)	OR	95% CI	P value	Probability of mortality (%)	95% CI
≤ 1	1			0.232	(0.152, 0.337)
1-2	1.04	(0.58, 1.85)	0.902	0.238	(0.169, 0.324)
2-3	1.21	(0.65, 2.26)	0.545	0.268	(0.211, 0.332)
3-4	1.24	(0.50, 3.11)	0.644	0.272	(0.172, 0.403)
4-5	1.20	(0.45, 3.18)	0.711	0.266	(0.142, 0.443)
5-6	0.82	(0.33, 2.05)	0.676	0.199	(0.088, 0.391)
> 6	0.94	(0.54, 1.63)	0.817	0.220	(0.190, 0.253)

Conclusions

- ❖ In conclusion, our study demonstrated that timing of antibiotic administration may be a marker of optimal care of patients, not a predictor of clinical outcome in the patients with community-acquired severe sepsis or septic shock.
- ❖ Namely, a single factor does not appear to be an intervention factor to control the outcomes of them.
- ❖ Simply to attain compliance with the metrics of qualified-care, careless use of broad-spectrum antibiotics may cause potential detrimental effects on antibiotic stewardship and adverse events, but no reasonable gain.