

Analysis of Structure Indicators Influencing 3-h and 6-h Compliance with the Surviving Sepsis Campaign Guidelines in China: A Systematic Review

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Abstract

Background: Compliance with the surviving sepsis campaign (SSC) guidelines (C_{SSC}) is a key factor affecting the effects of sepsis treatment. We designed this study to investigate the relationships of the structure indicators of ICU on 3-h and 6-h C_{SSC} in China. A total of 1854 hospitals were enrolled in a survey, led by the China National Critical Care Quality Control Center (China-NCCQC) from January 1, 2018, through December 31, 2018.

Methods: We investigated the 1854 hospitals' 3-h and 6-h C_{SSC} , including compliance with each specific measure of the 3-h and 6-h SSC bundles. We also investigated the actual level of the structure indicators of ICU, released by China-NCCQC in 2015. The outcomes were in adherence with the SSC guidelines (2016). Monitoring indicators included 3-h and 6-h C_{SSC} .

Results: In the subgroup, the rate of broad-spectrum antibiotic therapy was the highest, and the rate of CVP and ScvO₂ measurement was the lowest. Structure indicators related to 3-h and 6-h C_{SSC} include the predicted mortality rate and the standardized mortality ratio (SMR). The relationships between 3-h and 6-h C_{SSC} and the proportion of ICU in total inpatient bed occupancy, the proportion of acute physiology and chronic health evaluation (APACHE) II score ≥ 15 in all ICU patients were uncertain. There was no relationship of 3-h and 6-h C_{SSC} with the proportion of ICU patients among total inpatients.

Conclusions: Structure indicators influencing 3-h and 6-h C_{SSC} in China are the predicted mortality rate and the standardized mortality rate.

Background

Sepsis 3.0 is defined as downregulation of host response after infection and the occurrence of life-threatening organ dysfunction (1, 2). The overall global burden of sepsis has increased over the past several decades. Although recent studies have shown that the mortality from sepsis can be reduced by compliance with the surviving sepsis campaign (SSC) guidelines (C_{SSC}) (3–5), the C_{SSC} in clinical work is only approximately 30% – 60%, which is far less than people's expectations.

The structure indicators of intensive care unit (ICU) reflect whether the resource allocation of the ICU meets the requirements. We assume that the structure indicators will have an important impact on the C_{SSC} . Therefore, the aims of this study were the following: 1. to investigate the C_{SSC} and structure indicators of ICU in China; and 2. determine the relationships between the C_{SSC} and structure indicators of ICU.

Methods

Hospitals

In 2018, 1854 hospitals in China were involved (Fig. 1). The total number of secondary and tertiary hospitals registered was 7525 across the country in 2018. China National Critical Care Quality Control Center (China-NCCQC) collected detailed data regarding quality control indicators through the database of the National Clinical Improvement System (<https://icuqc.console.clinify.cn/dataMonitoring>). The data were collected between January 1, 2018 and December 31, 2018. All of the information from participating hospitals is listed in Table 1 and Supplement 1. The 3-h and 6-h C_{SSC} are listed in Table 2 and Supplement 2 and 3.

Table 1
Basic information of different types of hospitals.

	Hospitals	Beds _{hos}	Beds _{ICU}	Patients _{hos}	Patients _{ICU}	Days _{hos}	Days _{ICU}	Doctors _{ICU}	Nurses _{ICU}
Public									
General									
Tertiary	877	1246054	25054	49534487	1052682	449420159	7177717	13439	47193
Secondary	698	389854	6777	15164592	285984	226320512	14097614	3991	11558
Specialized									
Tertiary	153	111351	4717	5921433	206430	49887588	1654392	2250	6819
Secondary	21	3369	368	195704	16176	1619987	75098	156	379
Private									
General									
Tertiary	41	39346	725	1389714	25114	15842900	157202	320	1135
Secondary	58	25768	507	907210	18440	7701873	118324	273	815
Total	1848	1815742	38148	73113140	1604826	750793019	23280347	20429	67899

Beds_{hos} = hospital beds, Beds_{ICU} = ICU beds, Patients_{hos} = Patients admitted in hospitals, Patients_{ICU} = Patients admitted in ICUs, Days_{hos} = Days of hospital bed occupancy by patients, Days_{ICU} = Days of ICU bed occupancy by patients, Doctors_{ICU} = ICU doctor number, Nurses_{ICU} = ICU nurse number. There are 6 private specialized hospitals, including 4 tertiary hospitals and 2 secondary hospitals which are not included in this table.

Table 2
Compliance of surviving sepsis campaign (SSC) guidelines (C_{SSC}) of different types of hospitals.

		3 h C _{SSC}	3 h C _{SSC-lac}	3 h C _{SSC-cul}	3 h C _{SSC-spe}	3 h C _{SSC-res}	6 h C _{SSC}	6 h C _{SSC-rep}	6 h C _{SSC-vas}	6 h C _{SSC-CVP}
Public										
General										
	Tertiary	0.75	0.82	0.75	0.85	0.78	0.64	0.66	0.66	0.49
	Secondary	0.75	0.79	0.74	0.83	0.75	0.63	0.65	0.65	0.49
Specialized										
	Tertiary	0.70	0.76	0.70	0.80	0.74	0.59	0.67	0.67	0.52
	Secondary	0.68	0.86	0.78	0.91	0.79	0.64	0.79	0.70	0.56
Private										
General										
	Tertiary	0.76	0.78	0.72	0.87	0.79	0.68	0.61	0.57	0.46
	Secondary	0.68	0.82	0.83	0.89	0.84	0.63	0.72	0.68	0.50
Total		0.74	0.80	0.74	0.84	0.77	0.63	0.66	0.66	0.50
SSC = surviving sepsis campaign, C _{SSC} = compliance of SSC guidelines, 3 h C _{SSC-lac} = completion of lactate concentration was determined, 3 h C _{SSC-cul} = completion of appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy, 3 h C _{SSC-spe} = completion of empiric broad-spectrum therapy, 3 h C _{SSC-res} = completion of resuscitation with 30 ml/kg crystal liquid, 6 h C _{SSC-rep} = completion of repeated measurement of lactate levels in patients with initial hyperlactatemia, 6 h C _{SSC-vas} = completion of resuscitation with vasopressor in patients with MAP ≤ 65 mmHg after fluid resuscitation, 6 h C _{SSC-CVP} = completion of CVP and ScvO ₂ were measured in patients with lactate ≥ 4 mmol/L.										

Study Design

In this study, the structure indicators of ICU were evaluated according to the National Clinical Quality Control Indicators for Critical Care Medicine (2015 Edition) released by the China-NCCQC. Monitoring indicators included the proportion of ICU patients among total inpatients, the proportion of ICU patients out of total inpatient bed occupancy, the proportion of APACHE II scores ≥ 15 in all ICU patients, the predicted mortality rate and the standardized mortality ratio. Each indicator is divided into 4 grades according to the implementation. Each 25% from bad to good is divided into the lowest group, the lower group, the higher group, and the highest group.

The primary end points were the 3-h and 6-h C_{SSC}. Monitoring indicators included 3-h C_{SSC} (1. Completion of lactate concentration was determined, 2. Completion of appropriate routine microbiologic cultures [including blood] obtained before starting antimicrobial therapy, 3. Completion of empiric broad-spectrum therapy, 4. Completion of resuscitation with 30 mL/kg crystal liquid) and 6-h C_{SSC} (1. Completion of repeated measurement of lactate levels in patients with initial hyperlactatemia, 2. Completion of resuscitation with vasopressor in patients with mean arterial pressure [MAP] ≤ 65 mmHg after fluid resuscitation, 3. Completion of central venous pressure [CVP] and central venous oxygen saturation [ScvO₂] measured in patients with lactate ≥ 4 mmol/L).

According to the above levels, we investigated the relationships of the structure indicators of ICU on 3-h and 6-h C_{SSC} in patients with sepsis in China.

The study was conducted in accordance with the *Declaration of Helsinki* (as revised in 2013). The trial protocol was approved by the Central Institutional Review Board at Peking Union Medical College Hospital (NO.: S-K1297) and individual consent for this retrospective analysis was waived. The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Collection

In all of the participating clusters, data were obtained and entered into a web-based data entry system by a local, trained independent research coordinator who was not involved in the care of patients and who received compensation for this trial. Range checks were used to check for inconsistent or out-of-range data, prompting the user to correct or review data entries outside the predefined range. The system also provided predefined logic checks to identify errors or illogical data entries. A data quality meeting was held monthly to review all of the hospital enrollment records and registry data.

Data Analysis

Statistical analysis was performed using SPSS software, version 16.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was employed to check whether the data were normally distributed. The results are described as mean ± standard deviation. Comparisons between multiple groups were analyzed by one-way analysis of variance (ANOVA), and pairwise comparisons after ANOVA were conducted using the Tukey multiple comparisons test. All of the statistical tests were two-tailed, and a $P < 0.05$ was considered to be statistically significant.

Results

Correlations between the structure indicators of ICU and C_{SSC}

There was no relationship of 3-h and 6-h C_{SSC} with the proportion of ICU patients among total inpatients (Fig. 2A).

3-h C_{SSC} in the lower, higher and highest group of the proportion of ICU in total inpatient bed occupancy was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2B). However, same phenomenon was not observed in each sub-index of hour-3 bundle (Fig. 2B). At the same time, same phenomenon was not observed in hour-6 bundle (Fig. 2B). These results indicated that relationship between C_{SSC} and the proportion of ICU in total inpatient bed occupancy is uncertain and further research is needed.

In the lower, higher and highest group of the proportion of APACHE II scores ≥ 15 in all ICU patients, 3-h C_{SSC} was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2C). Completion of empiric broad-spectrum therapy in the lower and higher group was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2C). However, same phenomenon was not observed in hour-6 bundle, other sub-index of hour-3 bundle and sub-index of hour-6 bundle (Fig. 2C). These results indicated that relationship of 3-h and 6-h C_{SSC} with the proportion of APACHE II scores ≥ 15 in all ICU patients is uncertain, and further research is needed.

6-h C_{SSC} in the lower, higher and highest group of the predicted mortality rate was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2D). 6-h C_{SSC} in the higher and highest group was significantly higher than that in the lower group ($P < 0.05$) (Fig. 2D). 6-h C_{SSC} in the highest group was significantly higher than that in the higher group ($P < 0.05$) (Fig. 2D). Completion of each sub-index of hour-3 bundle in the lower, higher and highest group was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2D). Completion of each sub-index of hour-3 bundle in the higher and highest group was significantly higher than that in the lower group except completion of lactate concentration was determined in the higher group ($P < 0.05$) (Fig. 2D). Completion of each sub-index of hour-6 bundle in the higher and highest group was significantly higher than that in the lower group except completion of repeated measurement of lactate levels in patients with initial hyperlactatemia in the higher group ($P < 0.05$) (Fig. 2D). These results indicated that higher predicted mortality rate mean better C_{SSC} .

6-h C_{SSC} in the lower, higher and highest group of the standardized mortality ratio was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2E). 6-h C_{SSC} in the higher group was significantly higher than that in the lower group ($P < 0.05$) (Fig. 2E). Completion of each sub-index of hour-3 bundle in the lower, higher and highest group was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2E). Completion of repeated measurement of lactate levels in patients with initial hyperlactatemia in the lower, higher and highest group was significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2E). Completion of resuscitation with vasopressor in patients with MAP ≤ 65 mmHg after fluid resuscitation and completion of CVP and ScvO₂ were measured in patients with lactate ≥ 4 mmol/L in the higher and highest group were significantly higher than that in the lowest group ($P < 0.05$) (Fig. 2E). These results indicated that lower standardized mortality ratio mean better C_{SSC} .

Discussion

An ICU is an area in a hospital that has substantial levels of risk for morbidity and mortality. Patients experience an average of 1.75 medication errors each day while in the ICU (6). Improving the quality of care given to ICU patients is highly desirable. On March 15, 2012, the Ministry of Health approved that Peking Union Medical College Hospital establish China-NCCQC. The Quality Improvement of Critical Care Program, led by China-NCCQC, was initiated in 2015. This study is part of the above program. In our study, a multifaceted Q_{ICU} intervention was effective in improving 3-h and 6-h C_{SSC} in septic shock in China. Wang found that the C_{SSC} of emergency physicians is often hindered by the doctors' awareness and attitudes(7). In our study, 6-h C_{SSC} was lower than 3-h C_{SSC} . In the subgroup, completion of empiric broad-spectrum therapy was the highest, and completion of CVP and ScvO₂ measured in patients with lactate ≥ 4 mmol/L was the lowest, which might be why 6-h C_{SSC} is lower than 3-h C_{SSC} . The key to improving 6-h C_{SSC} and even the whole C_{SSC} is improving completion of CVP and ScvO₂ measured in patients with lactate ≥ 4 mmol/L. In the 3-h subgroup, completion of appropriate routine microbiologic cultures (including blood) before starting antimicrobial therapy was the lowest. The key to improve 3-h C_{SSC} is improving completion of appropriate routine microbiologic cultures (including blood) before starting antimicrobial therapy.

Specifically, 3-h and 6-h C_{SSC} is related to predicted mortality rate, standardized mortality ratio. 3-h and 6-h C_{SSC} was better when the predicted mortality rate was higher, and the standardized mortality ratio was lower. The higher that the predicted mortality rate is, the higher that the proportion of patients admitted to the ICU with severe diseases is. The lower that the standardized mortality ratio is, the higher that the diagnosis and treatment level in the ICU is(8–10). The combination of the above two indicators can fully reflect the medical level of an ICU. Higher levels lead to better C_{SSC} .

The relationship of 3-h and 6-h C_{SSC} with the proportion of ICU patients among total inpatient bed occupancy, the proportion of APACHE II score ≥ 15 in all ICU patients is uncertain. Interestingly, predicted mortality rate, which is closely related to APACHE II score is related to 3-h and 6-h C_{SSC} . This phenomenon might reflect the difference in test titers between the two indicators. When examining 3-h and 6-h C_{SSC} , predicted mortality rate might be a more effective indicator.

While the relationship of 3-h and 6-h C_{SSC} with the proportion of ICU patients among total inpatient bed occupancy is uncertain, there was no relationship of 3-h and 6-h C_{SSC} with the proportion of ICU patients among total inpatients. Reason for the above phenomenon may be that both the proportion of ICU patients among total inpatient bed occupancy and C_{SSC} are correlated with hospital treatment level, while the proportion of ICU patients among total inpatients is not correlated with hospital treatment level.

There are some limitations of our study. First, since only one year's of data was included in this study, the relationships of the structure indicators of ICU on 3-h and 6-h C_{SSC} could not be analyzed continuously and dynamically. Second, those hospitals enrolled from China-NCCQC might be more motivated to improve sepsis care quality than other hospitals. Further studies will be necessary to determine the relationships of the structure indicators of ICU on 3-h and 6-h C_{SSC} in hospitals in China that differ in characteristics from those that participated.

Conclusions

The key to improving 6-h C_{SSC} and even the whole C_{SSC} is to improve completion of CVP and ScvO₂ being measured in patients with lactate ≥ 4 mmol/L. The key to improve 3-h C_{SSC} is to improve completion of appropriate routine microbiologic cultures (including blood) before starting antimicrobial therapy. The factors influencing 3-h and 6-h C_{SSC} in China are the predicted mortality rate and the standardized mortality ratio.

Abbreviations

surviving sepsis campaign = SSC, compliance with the surviving sepsis campaign guidelines = C_{SSC} , intensive care unit = ICU, China National Critical Care Quality Control Center = China-NCCQC, mean arterial pressure = MAP, central venous pressure = CVP, central venous oxygen saturation = ScvO₂.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the *Declaration of Helsinki* (as revised in 2013). The trial protocol was approved by the Central Institutional Review Board at Peking Union Medical College Hospital (NO.: S-K1297) and individual consent for this retrospective analysis was waived. The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Consent for publication

All authors have seen and agreed with the contents of the manuscript, and the manuscript has been submitted solely to this journal and is not published, in press, or submitted elsewhere.

Availability of data and material

The datasets supporting the conclusions of this article are included within the article and its additional files.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XZ, DWL & YL conceived and designed the experiments. LW, XDM, HWH, LXS, YHG & GLS analyzed the data, and wrote the manuscript. AND, LW, XDM & XZ edit and revised the manuscript. All authors read and approved the final manuscript.

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Figures

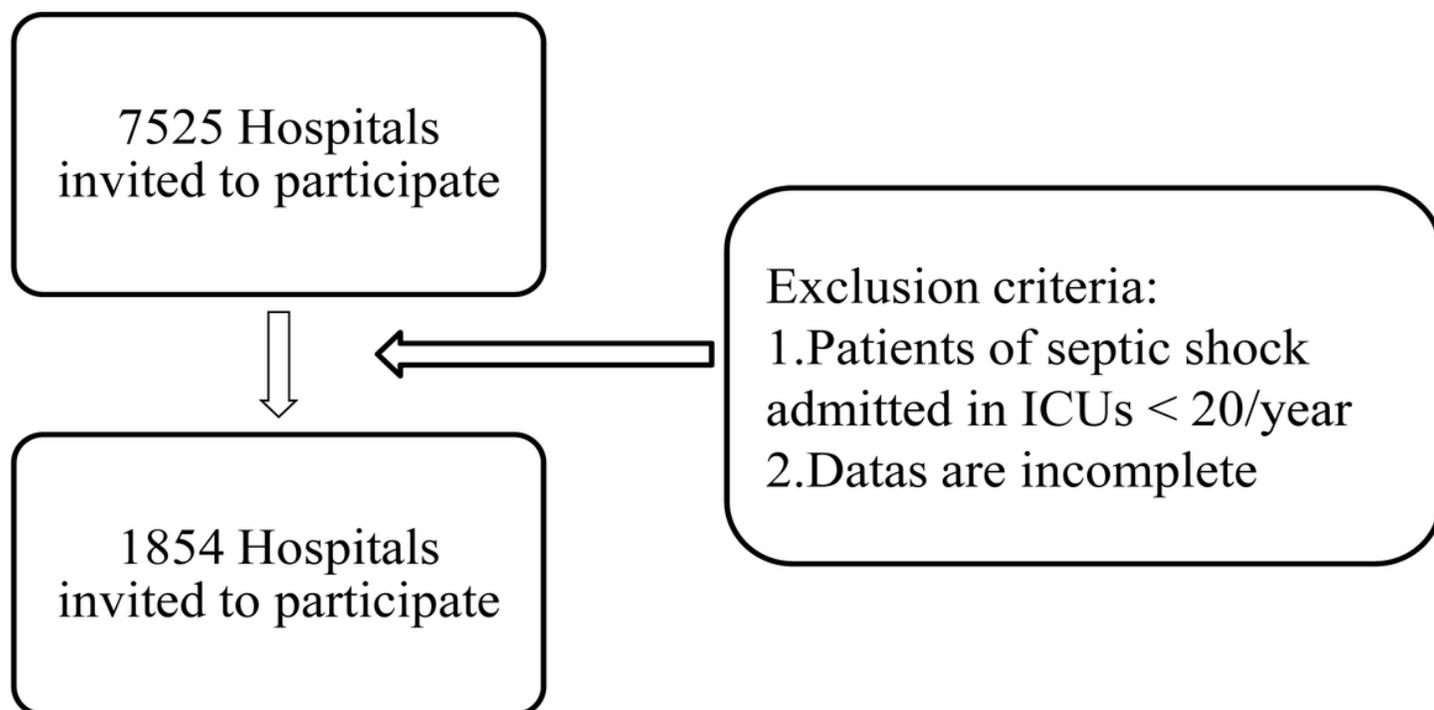


Figure 1

Flow of Hospitals through the Study.

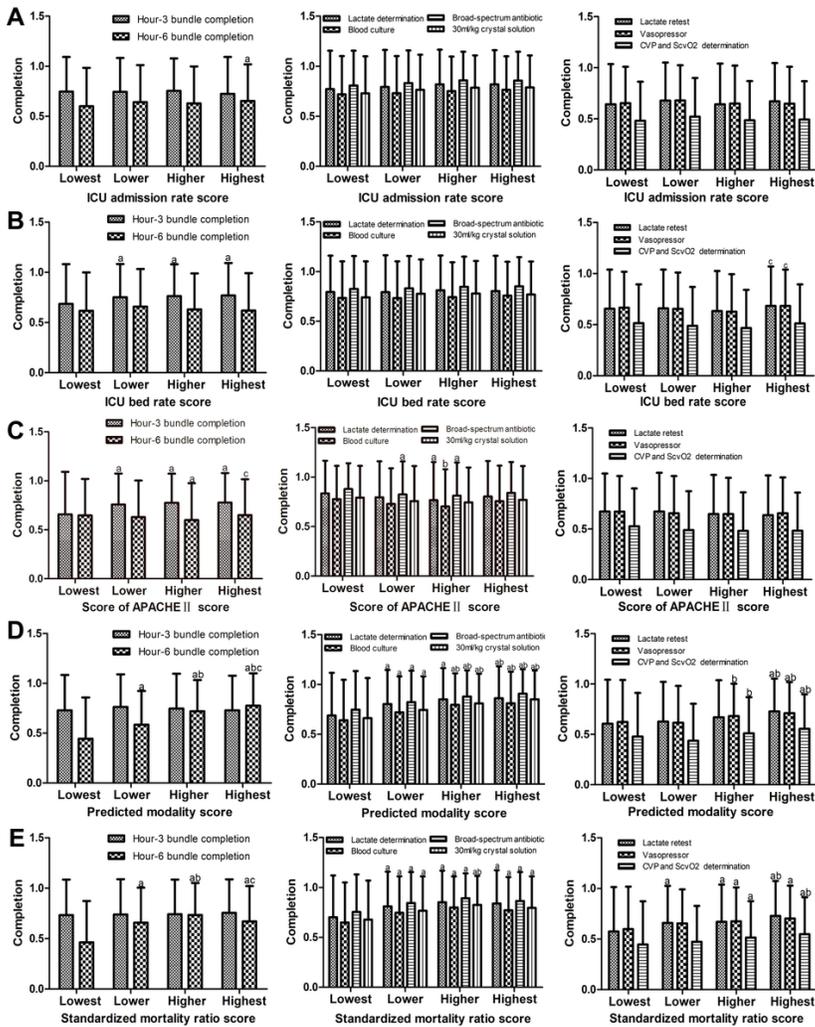


Figure 2

Correlation between the structure indicators and compliance of surviving sepsis campaign (SSC) guidelines (Cssc). Monitoring indicators included the proportion of ICU patients among total inpatients, the proportion of ICU patients out of total inpatient bed occupancy, the proportion of APACHE II scores ≥ 15 in all ICU patients, the predicted mortality rate and the standardized mortality ratio. Each indicator is divided into 4 grades according to the implementation. Each 25% from bad to good is one level, with 0, 1, 2, or 3 points. According to the scores, they are divided into the lowest group, the lower group, the higher group, and the highest group. Results are presented as mean \pm SD. a = $P < 0.05$ compared to the lowest group, b = $P < 0.05$ compared to the lower group, c = $P < 0.05$ compared to the higher group. DVT = deep vein thrombosis. ICU = intensive care unit. ICU admission rate = the proportion of ICU patients among total inpatients, ICU bed rate = the proportion of ICU patients out of total inpatient bed occupancy, APACHE II score = the proportion of APACHE II scores ≥ 15 in all ICU patients, Predicted mortality = the predicted mortality rate, Standardized mortality ratio = the standardized mortality ratio.

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