

脓毒症休克 液体复苏的得与失

中日友好医院急诊科
张国强



病例

- 王××，男性，75岁，病历号7354
- 主诉：发热伴咳嗽咳痰，少尿4日
- BP:90/60mmHg T:38.7℃ HR:145次/分
HR:28次/分 SaO₂:92% 神情恍惚，双肺
可及明显湿罗音；
- WBC 18.67×10⁹/L，NEUT 16.67×10⁹/L，
N% 86.9%，
乳酸：5.7mmol/L SvO₂: 47%
胸片：双肺多发斑片状渗出影



液体复苏的思考

◆液体复苏的概述

◆液体复苏的体会

◆液体复苏的思考



概述

- 脓毒症：感染+SIRS
- 严重脓毒症：感染伴有器官血流灌注不足或功能障碍
- 脓毒症休克：尽管适当的液体复苏仍然存在脓毒症诱发的低血压

流行病学

➤ 全球 **1800万例/年**，每年增加**1.5%**

脓毒症患者院内总体死亡率 **28.6%**

严重脓毒症和脓毒症休克患者死亡率
分别为**25-30%**和**40-70%**

液体复苏

- 严重脓毒症和脓毒症休克患者都存在一定的绝对或相对的有效**血容量不足**，因此需要尽快补充血容量

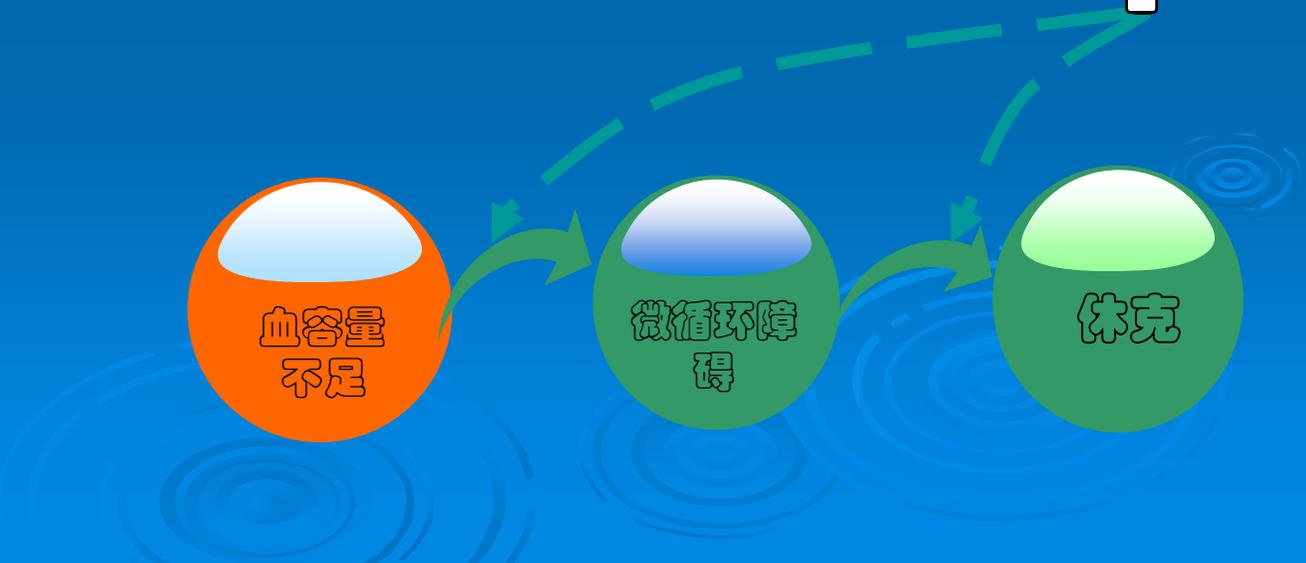


TABLE 3. KAPLAN-MEIER ESTIMATES OF MORTALITY AND CAUSES OF IN-HOSPITAL DEATH.*

VARIABLE	STANDARD THERAPY (N = 133)	EARLY GOAL-DIRECTED THERAPY (N = 130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	29 (42.3)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03
Causes of in-hospital death‡				
Sudden cardiovascular collapse	25/119 (21.0)	12/117 (10.3)	—	0.02
Multiorgan failure	26/119 (21.8)	19/117 (16.2)	—	0.27

*CI denotes confidence interval. Dashes indicate that the relative risk is not applicable.

†Percentages were calculated by the Kaplan–Meier product-limit method.

‡The denominators indicate the numbers of patients in each group who completed the initial six-hour study period.

Rivers E, et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001, 345(19):1368-1377

**2008年关于严重脓毒血症和脓毒血症休
克的管理指南**

**Surviving Sepsis Campaign
international guidelines for
management of severe sepsis and
septic shock 2008**

EGDT推荐级别 1C



EGDT

在早期复苏最初6小时内的复苏目标包括：

- ① 中心静脉压 (CVP) 8~12cmH₂O;
- ② 90mmHg > 平均动脉压 (MAP) ≥ 65mmHg;
- ③ 中心静脉 (上腔静脉) 氧饱和度(SCVO₂) ≥ 70%

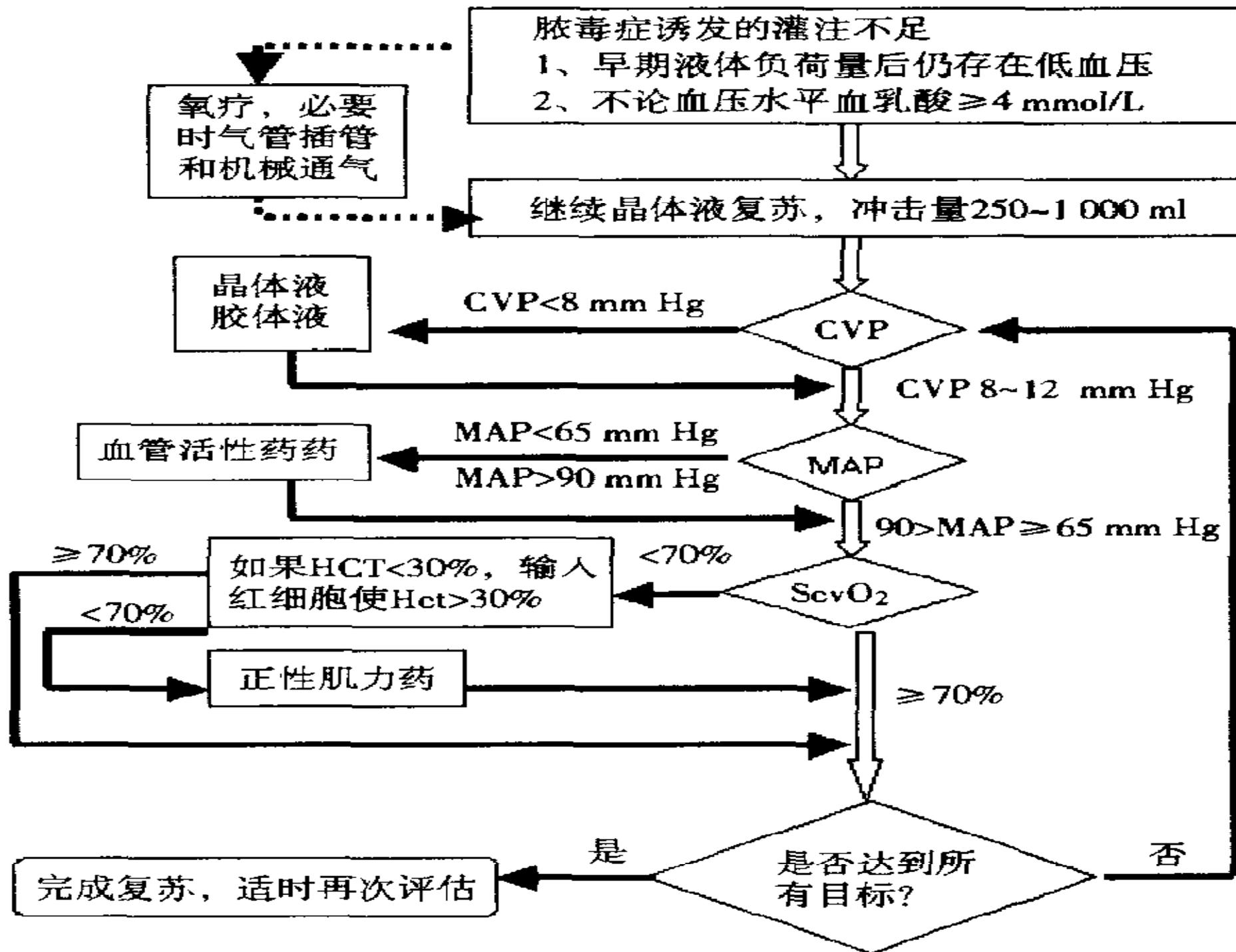
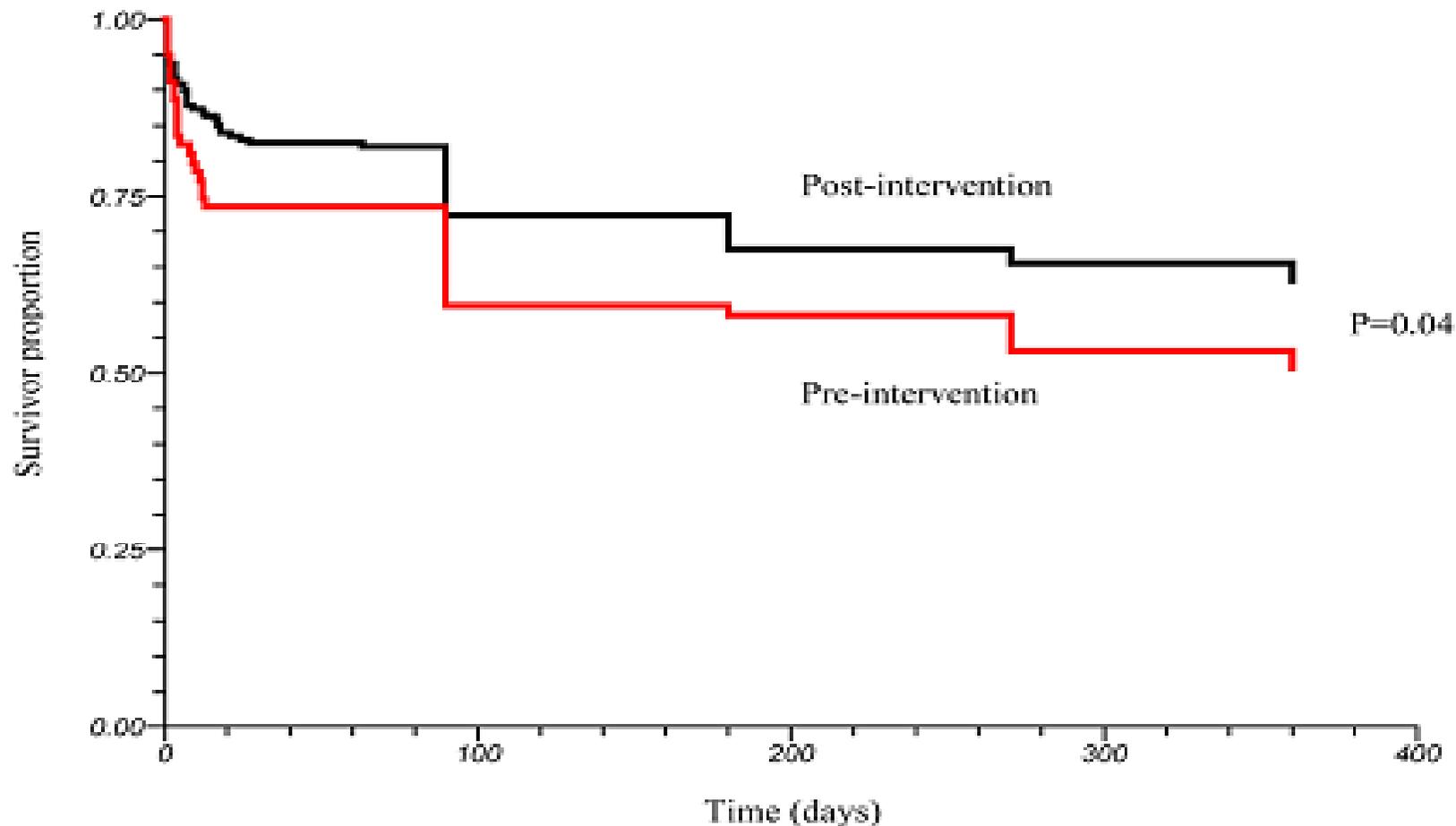


Figure 1



Kaplan Meier survival curve comparing survival of patients in the pre-implementation and post-implementation phases. The P value shown was derived from the log-rank test.

Puskarich MA, et al. One year mortality of patients treated with an emergency department based early goal directed therapy protocol for severe sepsis and septic shock: a before and after study. *Critical Care* 2009, 13:R167

液体复苏的思考

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病例1

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➤ 治疗：

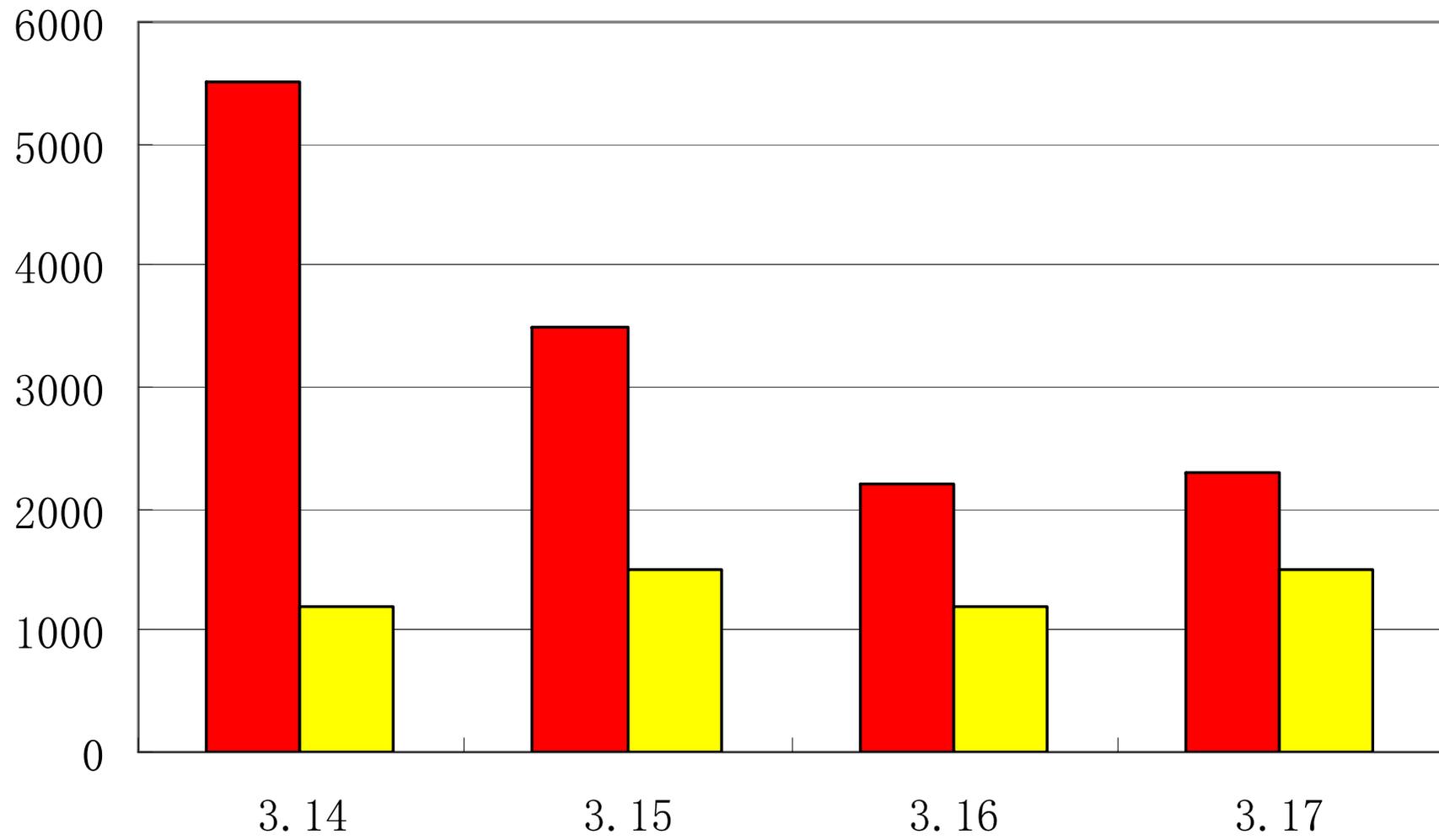
行深静脉穿刺，测CVP 4cmH₂O

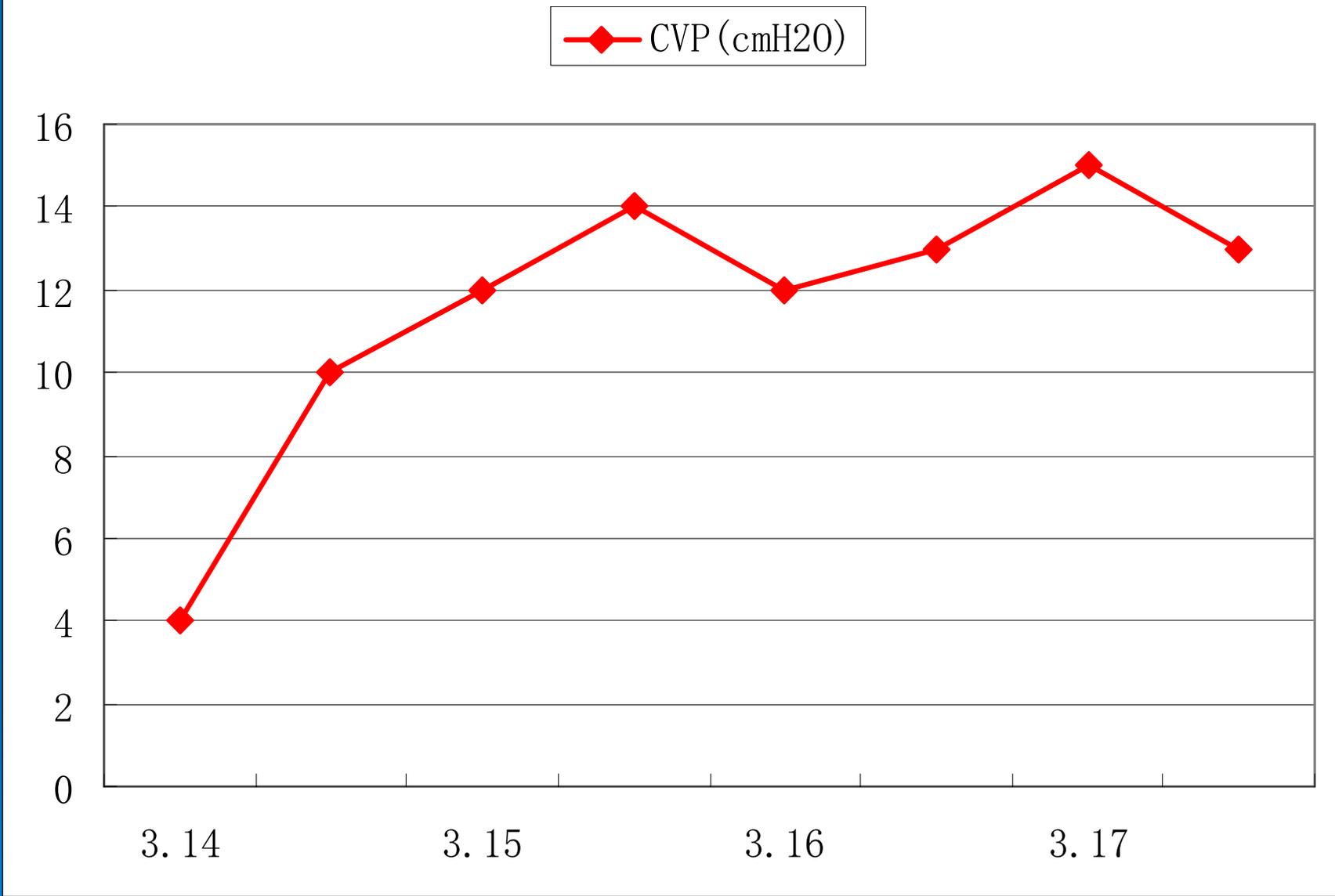
快速补液

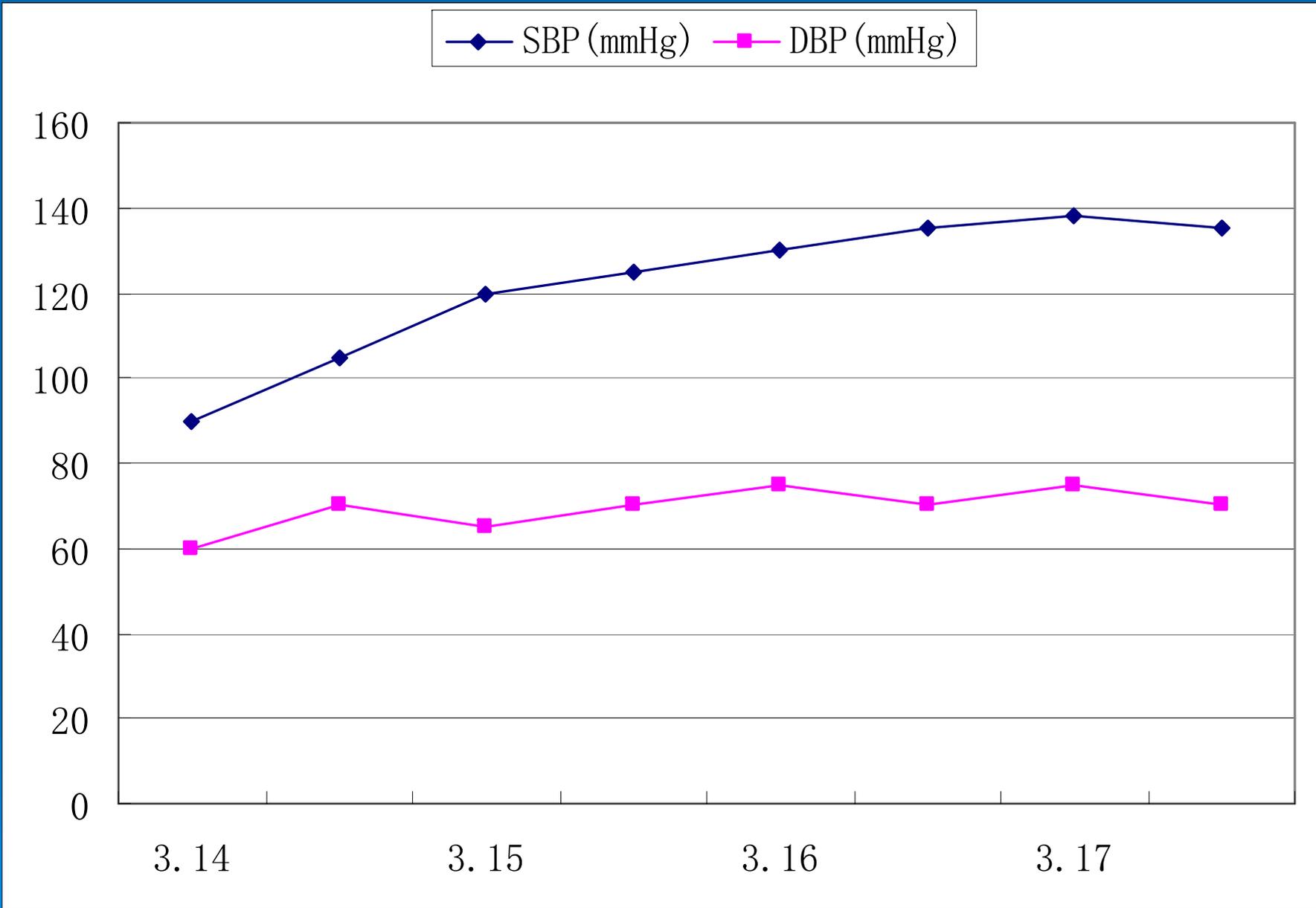
抗感染

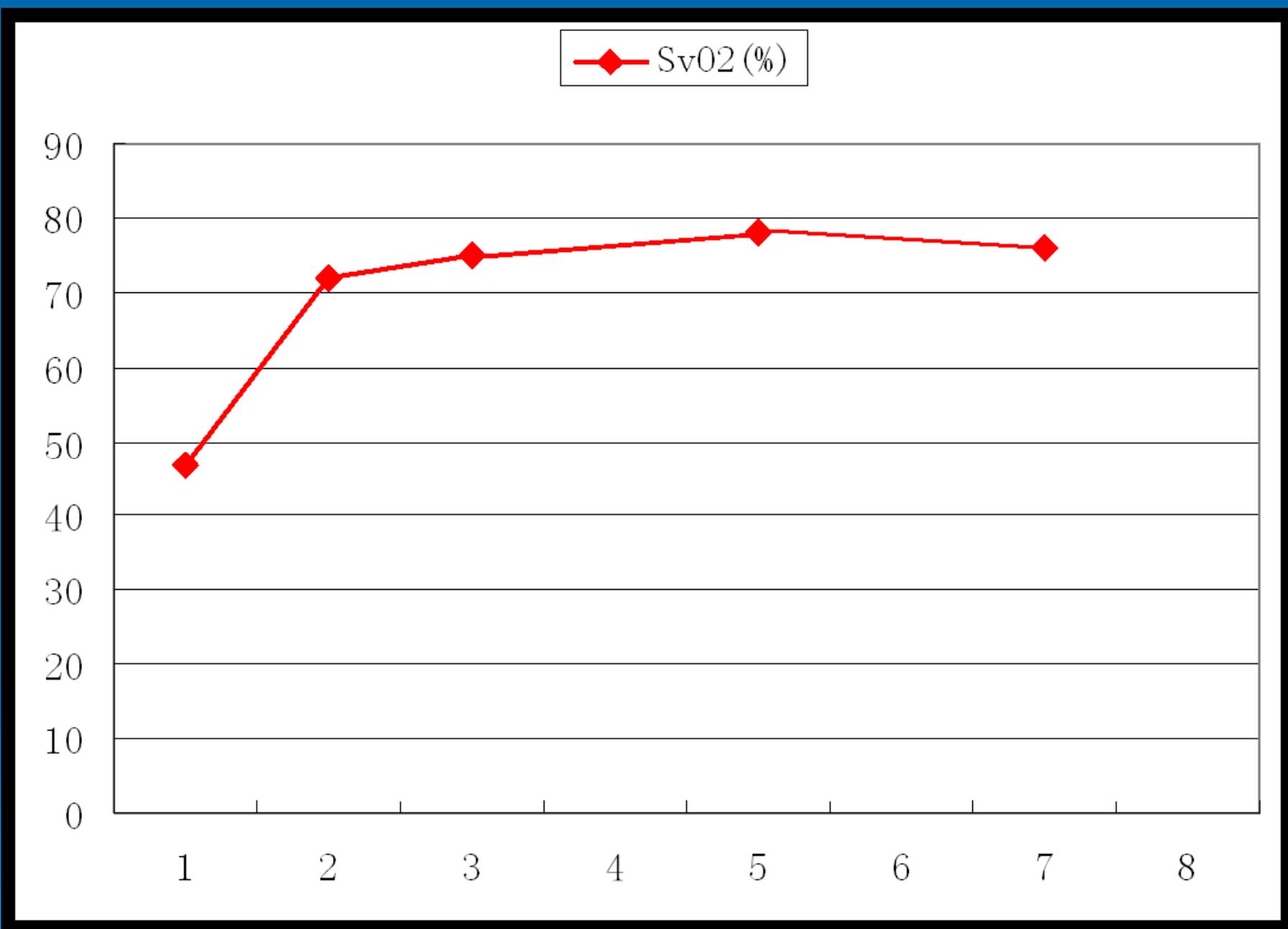
支持治疗

■ 入量 (ml) □ 出量 (ml)

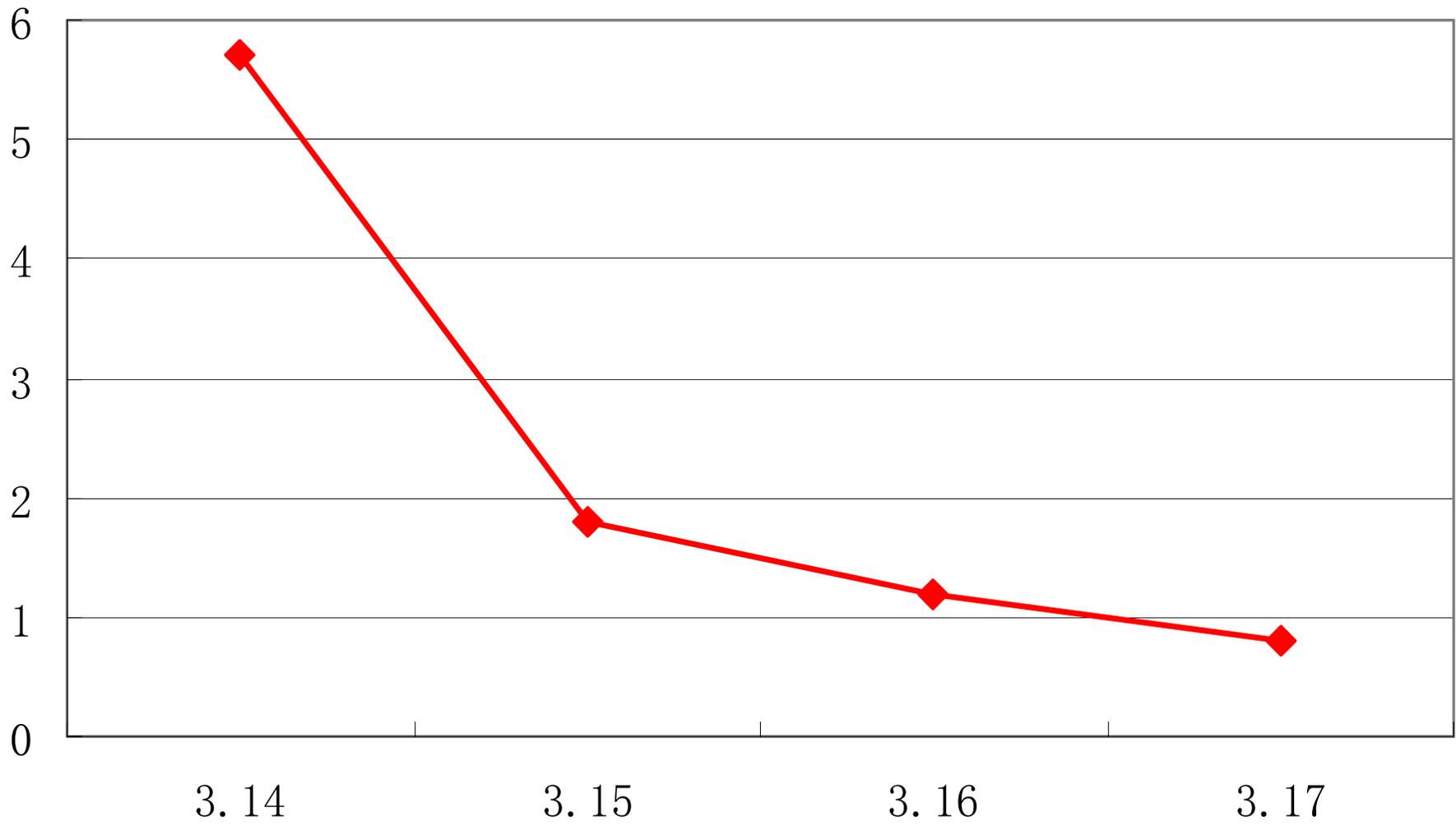








—◆— 乳酸 (mmol/L)



➤ 患者症状逐渐缓解，二周后出院

病例2

- 患者，女，31岁
- 入院时间：2011年4月21日
- 主诉：静脉输“美白”药物中发热、心悸4小时.患者网购“美白”药物，4小时前静点时出现发热，体温最高40℃，伴寒战，伴心悸、胸闷，伴全身发红，无皮疹，

病例2

➤ 既往：青霉素类药物过敏

➤ 体格检查： BP:80/47mmHg T:39.4℃
HR:118次/分 SaO₂:95%

神情

双肺呼吸音粗，未闻及明显干湿罗音，腹软，腹部无明显压痛及反跳痛，肠鸣音2-3次/分

➤ 辅助检查:

血常规: **WBC $1.5 \times 10^9/L$, NEUT $1.09 \times 10^9/L$, N% 72.7%**,

血气分析 **HCO₃⁻: 13mmol/L BE: -10.1mmol/L 乳酸: 6.5mmol/L**

PCT: 66.28ng/ml BNP: 32.2pg/ml

胸片: 双肺纹理增粗

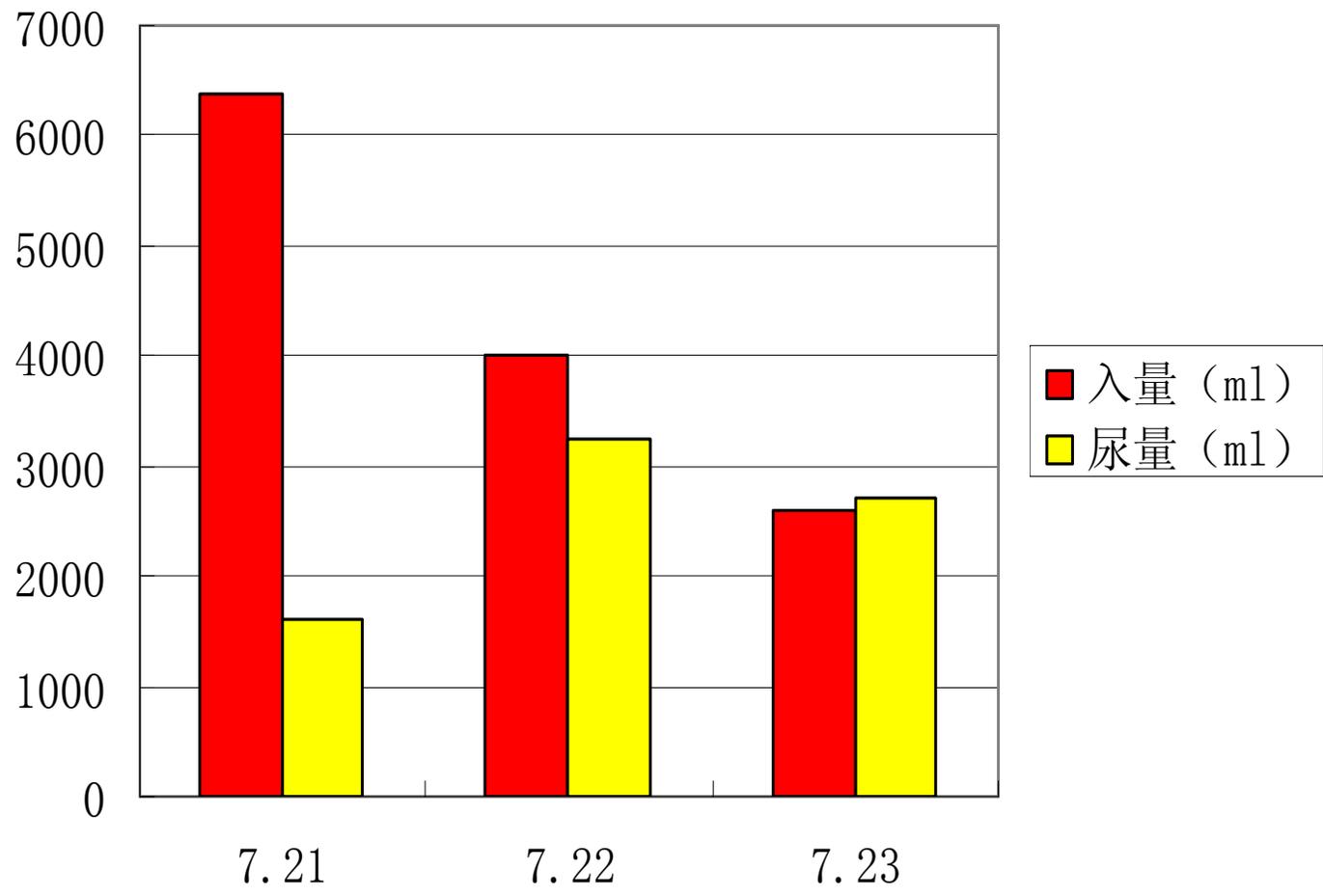
心电图: 窦性心动过速

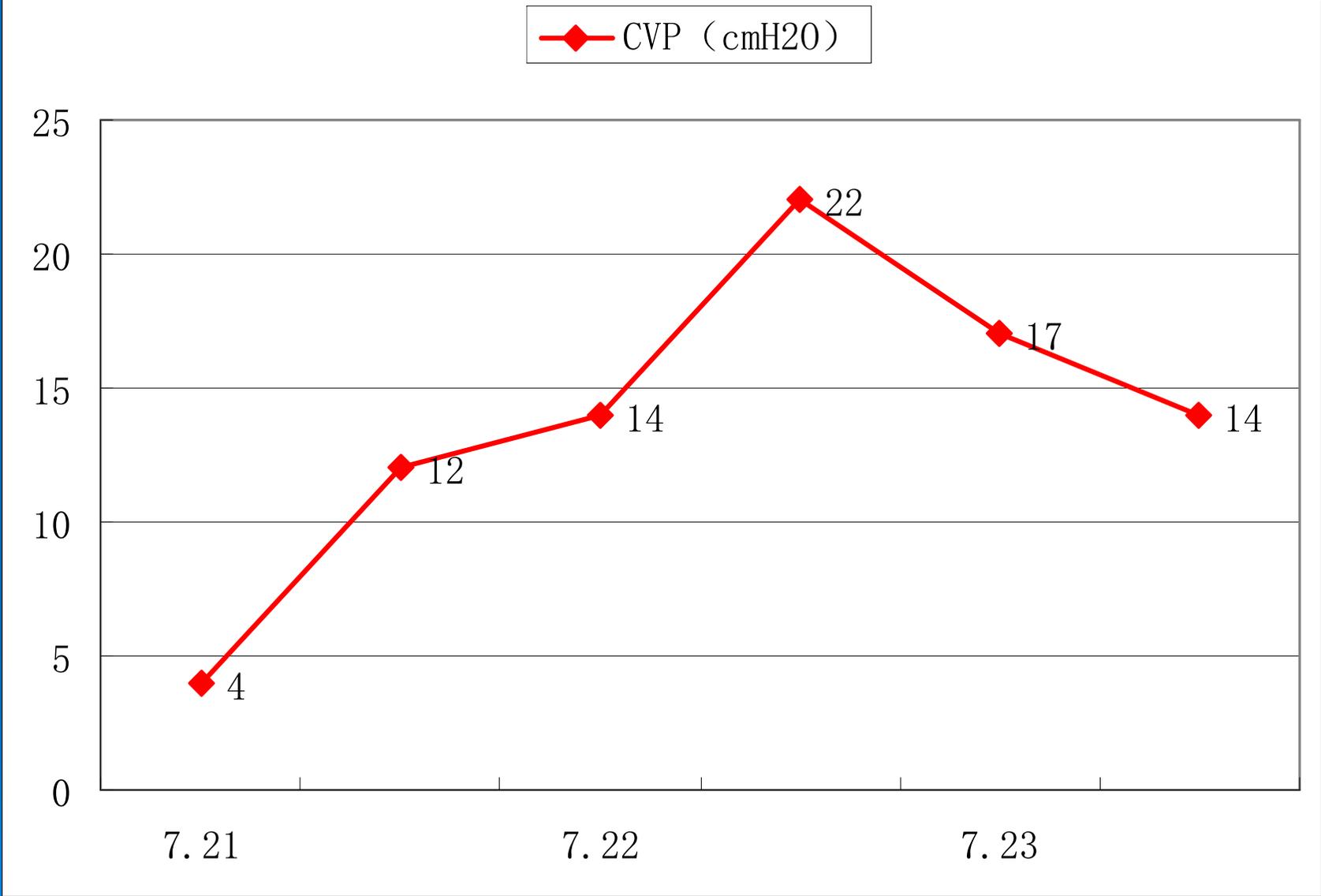
诊断和治疗

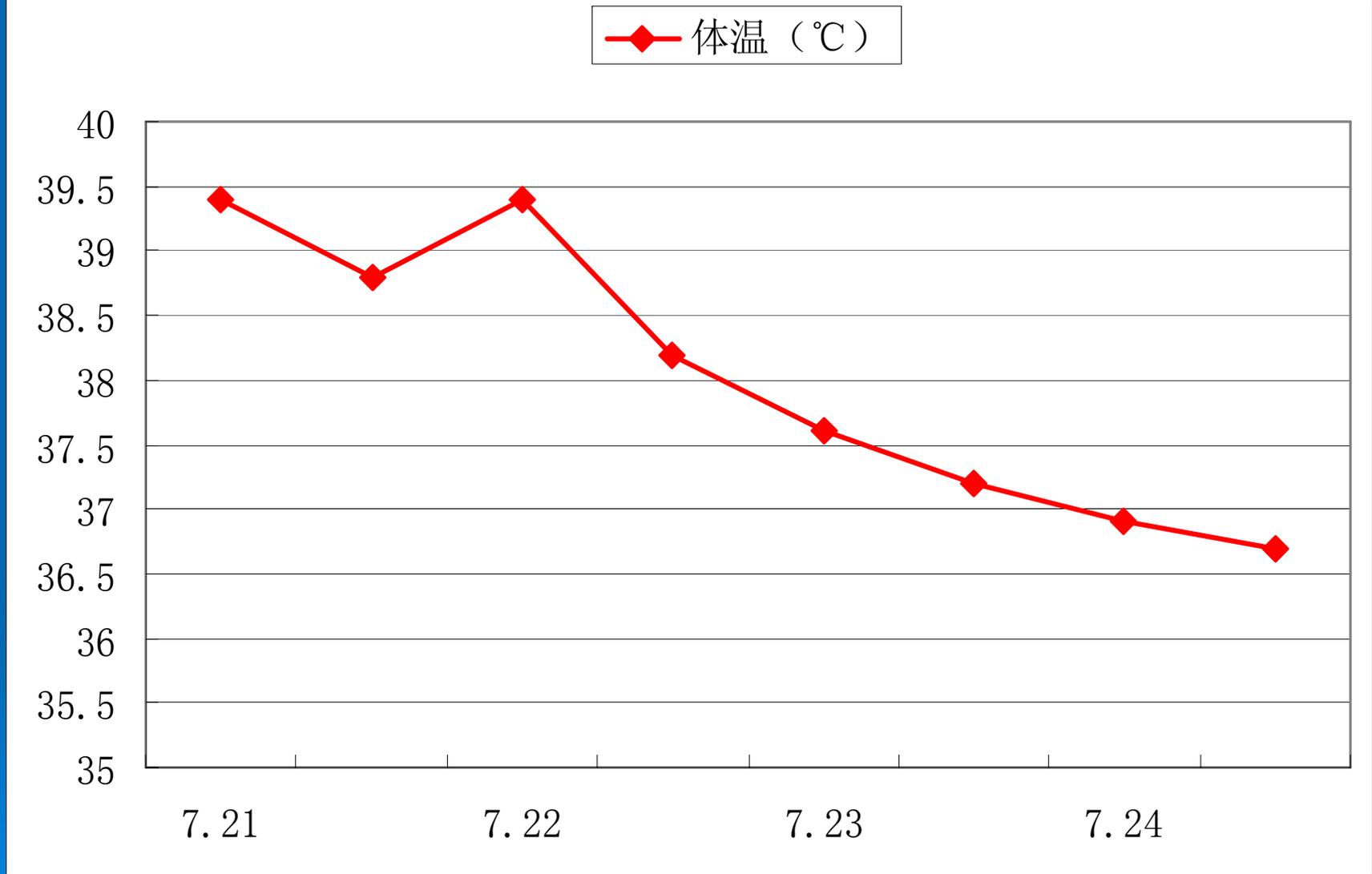
- 入院诊断：脓毒症休克
- 行深静脉穿刺，测CVP 4cmH₂O
- 快速补液
- 抗感染
- 支持治疗

- 患者于第二日开始出现胸闷憋气，四肢水肿明显，测CVP 22cmH₂O，复查BNP 447pg/ml
- 减少静脉液体量，减慢输液速度，少量利尿剂治疗，患者症状逐渐缓解

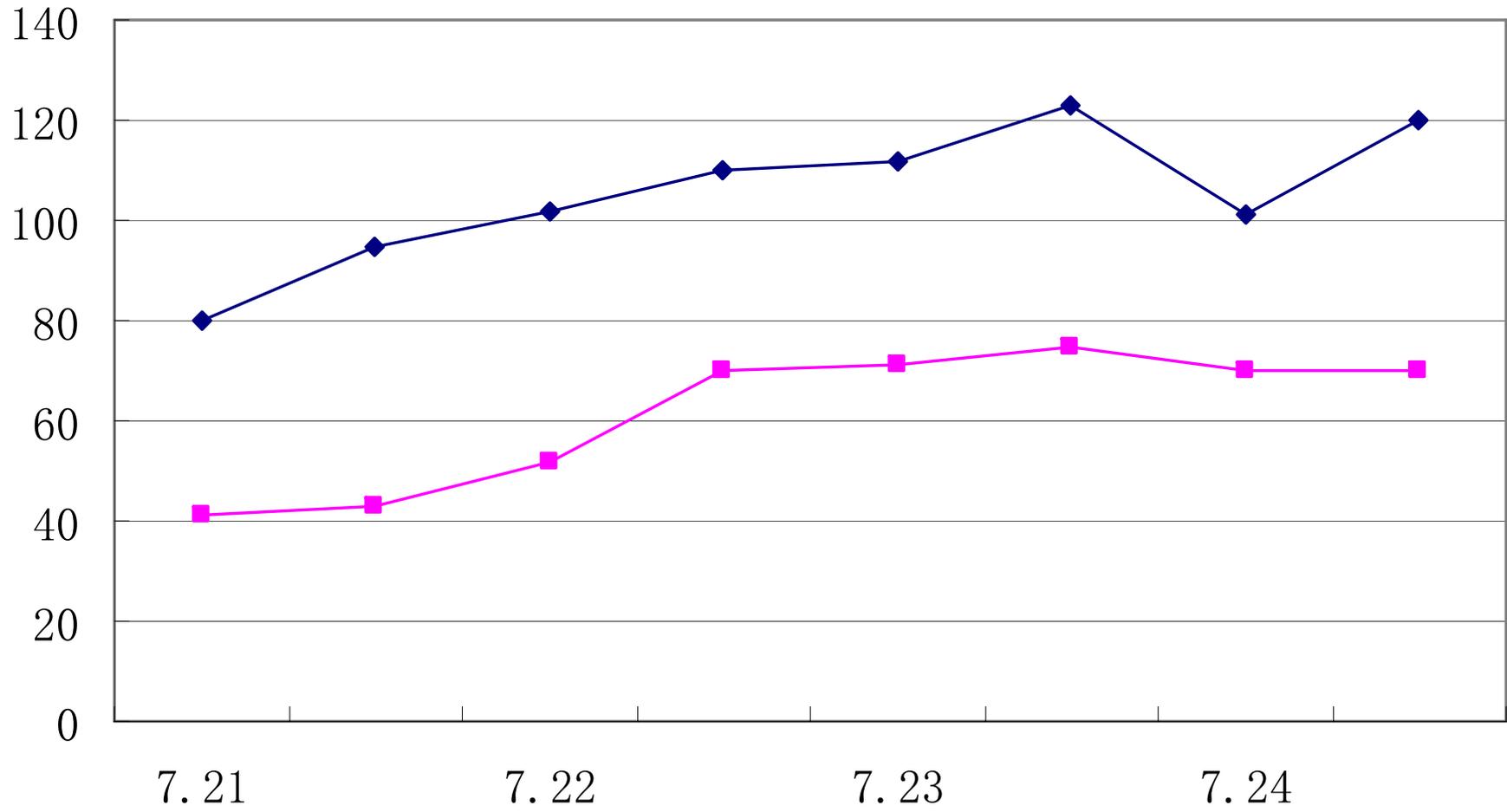
出入量

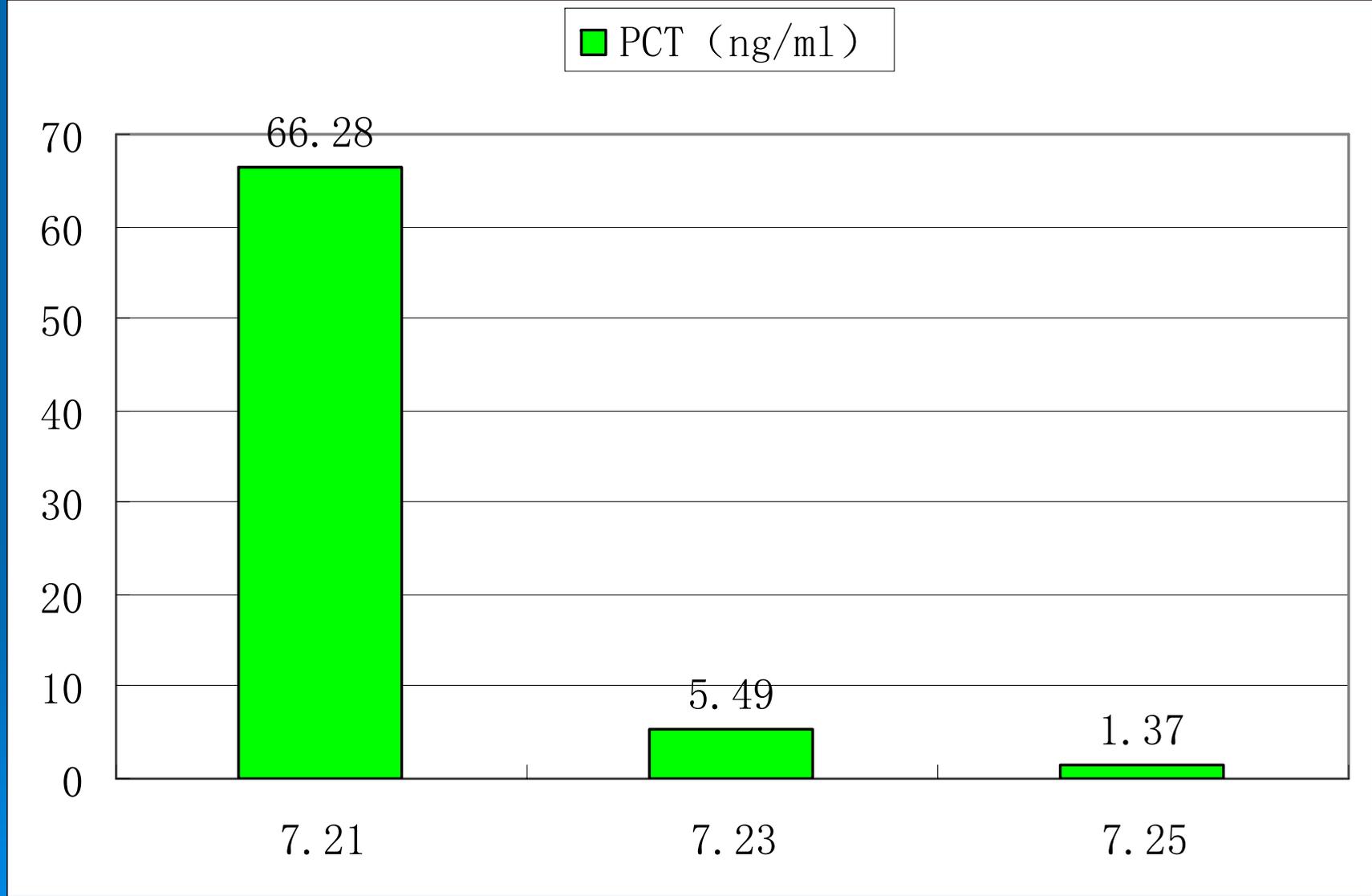






—◆— 收缩压 (mmHg) —■— 舒张压 (mmHg)





转归

- 患者症状逐渐缓解，体温正常，循环稳定，查超声心动图和心肌坏死标记物，于2011年7月28日出院

(血培养结果：肺炎克雷伯氏菌)

病例3

患者，女，44岁，

因“左腰背胀痛2月，加重伴发热2天”来
诊

查体：神清，BP96/59mmHg，HR110次/
分，R：20bpm，T 39

左肾区扣痛（+），余（—）。

WBC：14*10⁹/L N% 85% PLT 78*10⁹/L

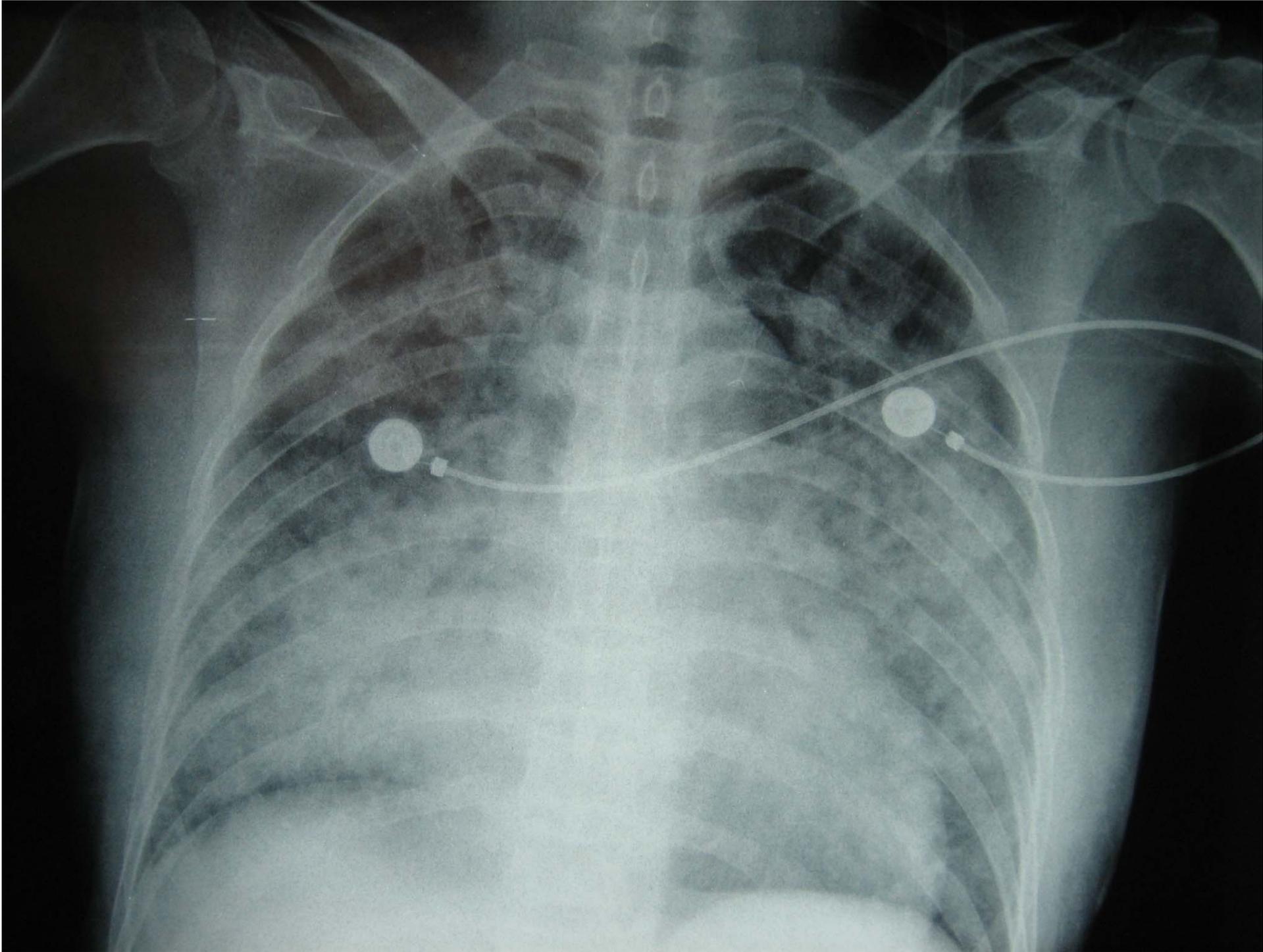
尿OB（++），WBC10/HP

BUS：左肾多发结石，左肾积水，左输尿
管结石，左输尿管扩张；

入院诊断

- 入院诊断:泌尿系结石伴感染
- 可乐必妥抗炎
补液:晶体液1500ml

- 患者入院后4小时出现胸闷、憋气症状，伴有咳嗽， SpO_2 80%，心率120-130次/分，双肺可闻及哮鸣音及湿罗音
- 查血气示: PH 7.26 PaO₂ 55mmHg
PaCO₂ 36mmHg
- 胸片示: 心影扩大，双肺弥漫性改变



- BNP: 2320pg/ml
- CVP : 23mmH₂O
- 超声心动图: 未见明显异常
- TNI : (-)

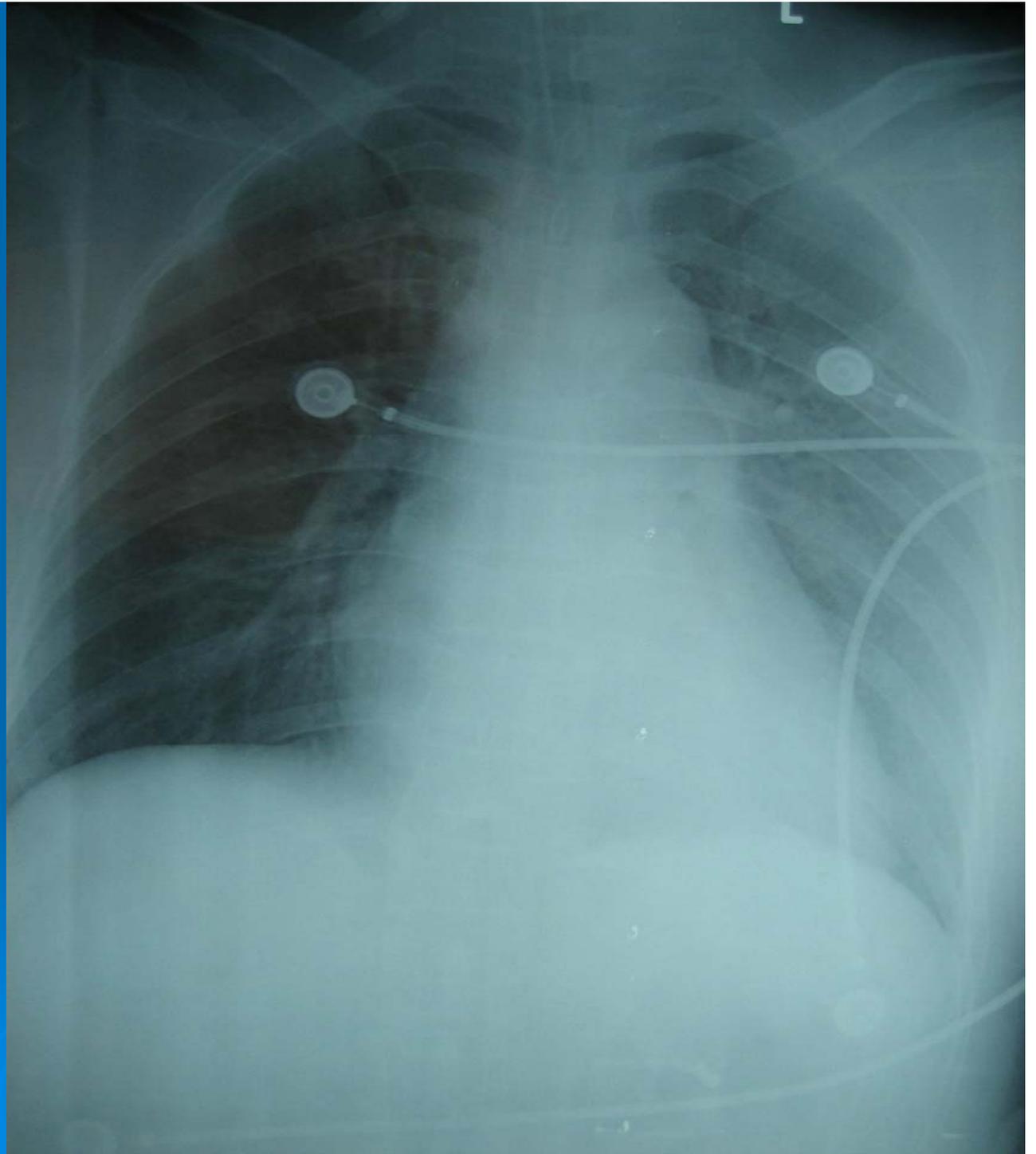
治疗

- 减少入量，加强利尿
- 给予呼吸机辅助呼吸， SpO_2 上升至90%
- 抗感染等(大肠杆菌)

转归

- 血压、心率平稳，一周后出院

4月3日



液体复苏的思考

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液体复苏的思考

◆复苏液体的选择

◆液体复苏的评价指标

◆EGDT的挑战



复苏液体的选择

晶体液：

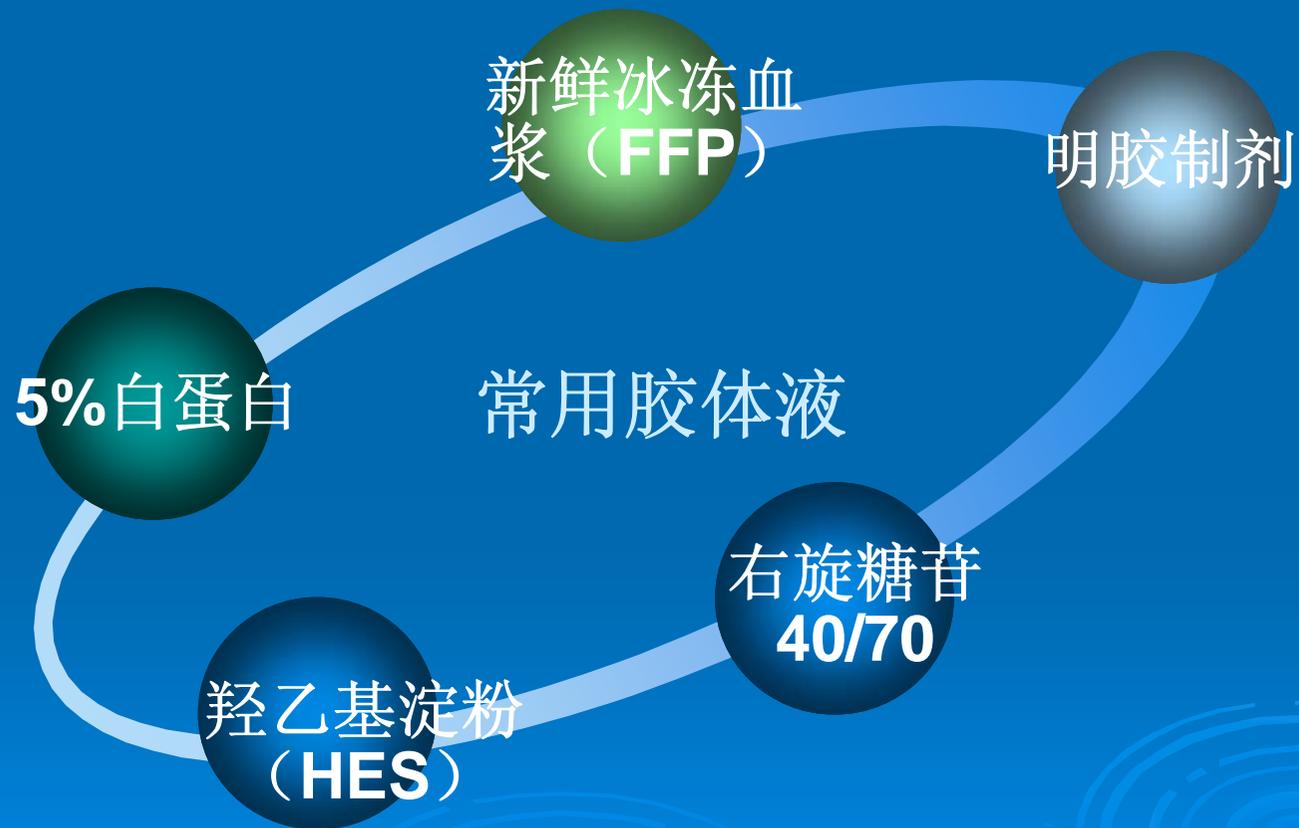
- 输注的晶体液会有80%迅速转移到血管外，进入组织间隙
- 为了恢复正常的血容量，需要输注4-5倍于失血量的晶体液
- 降低血浆胶体渗透压

复苏液体的选择

晶体液的早期扩容效果低于胶体液



复苏液体的选择



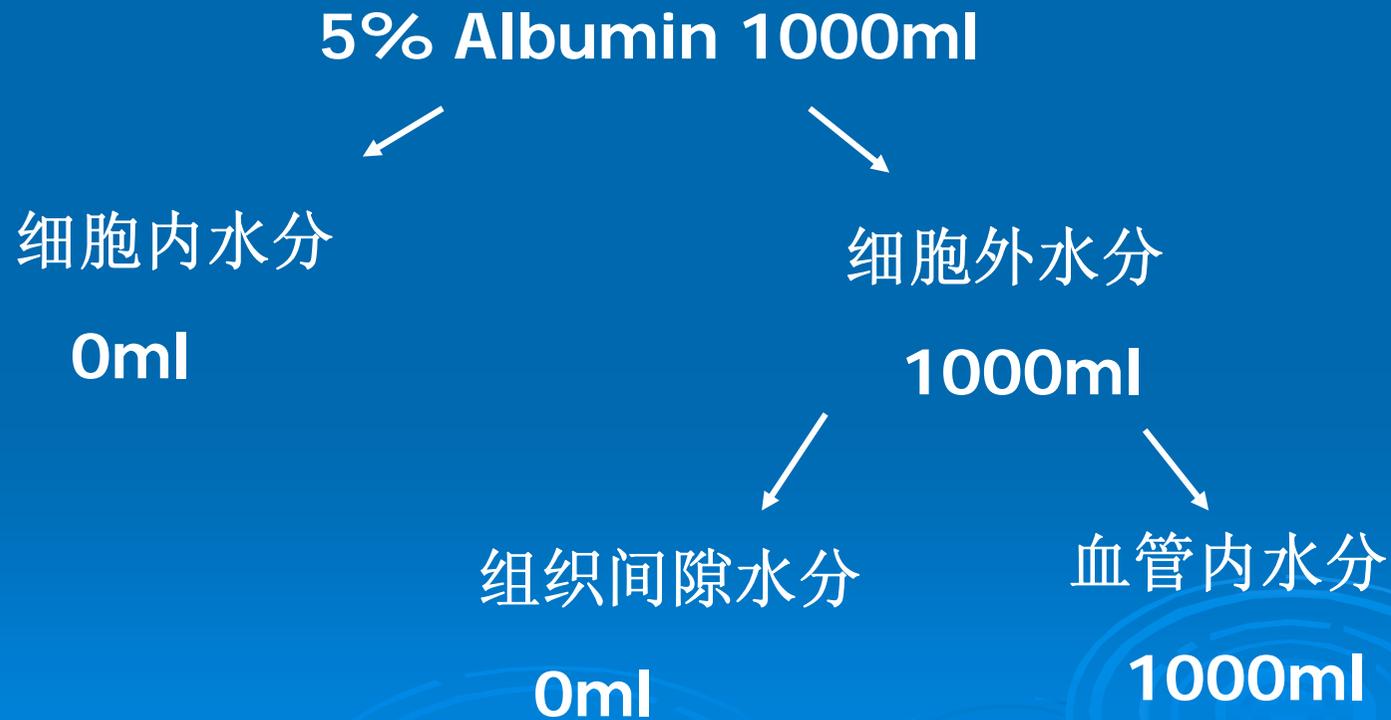
复苏液体的选择

胶体液：



复苏液体的选择

5%白蛋白 白输入后体内液体分布



复苏液体的选择

Table 3. Primary and secondary outcomes

	Hydroxyethyl Starch Group (n = 118)	<i>p</i>	Adjusted <i>p</i>	Gelatin Group (n = 87)	<i>p</i>	Adjusted <i>p</i>	Crystalloid Group (n = 141)
RIFLE risk, n (%) ^a	15 (13)	.698	1.000	10 (11)	.831	1.000	15 (11)
RIFLE injury, n (%) ^b	12 (10)	.842	1.000	14 (16)	.319	1.000	16 (11)
RIFLE failure, n (%) ^c	56 (47)	<.001	0.002	35 (40)	.018	.162	35 (25)
AKI, n (%) ^d	83 (70)	<.001	0.002	59 (68)	.003	.025	66 (47)
Renal replacement therapy, n (%)	40 (34)	.011	0.086	30 (34)	.019	.162	28 (20)
Sequential Organ Failure score maximum, median (IQR) ^e	11 (9–14)	.355	1.000	13 (10–15)	.332	1.000	12 (9–14)
Sequential Organ Failure score mean, median (IQR) ^e	7 (6–10)	.032	.227	8 (6–10)	.122	.853	8 (6–11)
Intensive care unit mortality, n (%)	41 (35)	.506	1.000	23 (26)	.550	1.000	43 (30)
Hospital mortality, n (%)	51 (43)	.311	1.000	27 (31)	.393	1.000	52 (37)
Intensive care unit length of stay, days, median (IQR)	14 (6–28)	.070	.421	13 (6–26)	.167	1.000	10 (5–20)

Ole Bayer, et al. Renal effect of synthetic colloids and crystalloids in patients with severe sepsis: A prospective sequential comparison. Crit Care Med 2011, 39(6):1335-1342

复苏液体的选择

Table 2. Total fluids and blood products administered during intensive care unit stay

	Hydroxyethyl Starch Group (n = 118)	Gelatin Group (n = 87)	Crystalloid Group (n = 141)
Total fluid amount, median (mL/kg) BW ^a (IQR)	649 (275–1098) ^b	525 (237–868)	355 (173–911)
Total amount of study fluids, median (mL/kg) BW (IQR)	46 (18–92) ^c	43 (18–76) ^d	105 (41–270)
Total amount of crystalloids, median (mL/kg) BW (IQR)	359 (206–619)	345 (216–649)	325 (180–636)
Blood products, median units (IQR)			
Fresh-frozen plasma	8 (4–16)	6 (4–12)	6 (4–12)
Platelet concentrates	3 (2–5) ^b	2 (1–3)	2 (1–3)
Red blood cells	2 (2–4)	2 (2–2)	2 (1–4)
Human albumin 20%, median (mL/kg) BW IQR	12 (5–24)	8 (5–27)	10 (4–19)

Ole Bayer, et al. Renal effect of synthetic colloids and crystalloids in patients with severe sepsis: A prospective sequential comparison. Crit Care Med 2011, 39(6):1335-1342

复苏液体的选择

Table 2. (Continued.)

Variable	Insulin Therapy			P Value†	Fluid Resuscitation		P Value‡
	All Patients (N = 537)	Conventional (N = 290)	Intensive (N = 247)		Ringer's Lactate (N = 275)	HES (N = 262)	
Hypoglycemia (≤40 mg/dl)				<0.001			0.85
No. of patients/total no.	54/537	12/290	42/247		27/275	27/262	
Percent (95% CI)	10.1 (7.5–12.6)	4.1 (1.9–6.4)	17.0 (12.3–21.7)		9.8 (6.3–13.3)	10.3 (6.6–14.0)	
Acute renal failure				0.25			0.002
No. of patients/total no.	153/533	77/289	76/244		62/272	91/261	
Percent (95% CI)	28.7 (24.9–32.6)	26.6 (21.6–31.7)	31.1 (25.3–37.0)		22.8 (17.8–27.8)	34.9 (29.1–40.7)	
Renal-replacement therapy				0.19			0.001
No. of patients/total no.	132/533	65/289	67/244		51/272	81/261	
Percent (95% CI)	24.8 (21.1–28.4)	22.5 (17.7–27.3)	27.5 (21.9–33.1)		18.8 (14.1–23.4)	31.0 (25.4–36.7)	

Brunkhorst FM, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med 2008, 358:125-139

复苏液体的选择

Table 2. Primary and Secondary Outcomes.*

Variable	Insulin Therapy			Fluid Resuscitation		P Value‡	
	All Patients (N=537)	Conventional (N=290)	Intensive (N=247)	Ringer's Lactate (N=275)	HES (N=262)		
Death							
At 28 days§						0.74	0.48
No./total no.	136/536	75/289	61/247	66/274	70/262		
Percent (95% CI)	25.4 (21.7–29.1)	26.0 (20.9–31.0)	24.7 (19.3–30.1)	24.1 (19.0–29.2)	26.7 (21.4–32.1)		
At 90 days						0.31	0.09
No./total no.	200/535	102/288	98/247	93/274	107/261		
Percent (95% CI)	37.4 (33.3–41.5)	35.4 (29.9–40.9)	39.7 (33.6–45.8)	33.9 (28.3–39.6)	41.0 (35.0–47.0)		

Brunkhorst FM, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med 2008, 358:125-139

复苏液体的选择

胶体液：

- 胶体液的早期扩容效果优于晶体液
- 胶体液可能会导致急性肾损伤（Acute Kidney Injury, AKI）
- 肾损伤作用与胶体液使用的剂量有关
- 胶体液扩容优势随着时间的延长会逐渐减退
- 胶体液不能改善脓毒症患者的预后

液体复苏的思考

- ◆ 复苏液体的选择
- ◆ 液体复苏的评价指标
- ◆ EGDT的挑战

液体复苏的评价指标

- 传统指标：血压、心率、休克指数、尿量、全身表现等

然而，休克的本质在于微循环障碍，单纯的血压并不能准确反映器官的灌注和代谢状况

“休克深藏于组织中，不可能仅通过听心音和测血压发现休克”

液体复苏的评价指标

➤ 评价指标：



下腔静脉变异率

患者处于低血容量状态时，下腔静脉随呼吸运动产生的管径变异会明显增加

$$\text{IVC变异率} = (\text{IVCmax} - \text{IVCmin}) / \text{IVCmax}$$

液体复苏评价指标



中心静脉压(CVP):8-12mmHg

反映心脏前负荷和心功能

- ① $< 8\text{mmHg}$, 心脏前负荷不够
- ② $\leq 12\text{mmHg}$, 心脏前负荷过多,或心功能不全

液体复苏的评价指标

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下腔静脉变异率

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液体复苏的评价指标

➤ 评价指标:



中心静脉压(CVP):8-12mmHg

< 8mmHg , 心脏前负荷不够

>12mmHg , 心脏前负荷过多,
或心功能不全

液体复苏前



液体复苏后



液体复苏的评价指标

➤ 评价指标:



血乳酸

组织氧供和氧需求失衡的间接反应，
大致能反映低灌注和休克的严重程度

参考值 $\leq 2\text{mmol/L}$

液体复苏的评价指标

➤ 评价指标

中心静脉血氧饱和度

反映内脏血管床的灌注和氧供氧需情况

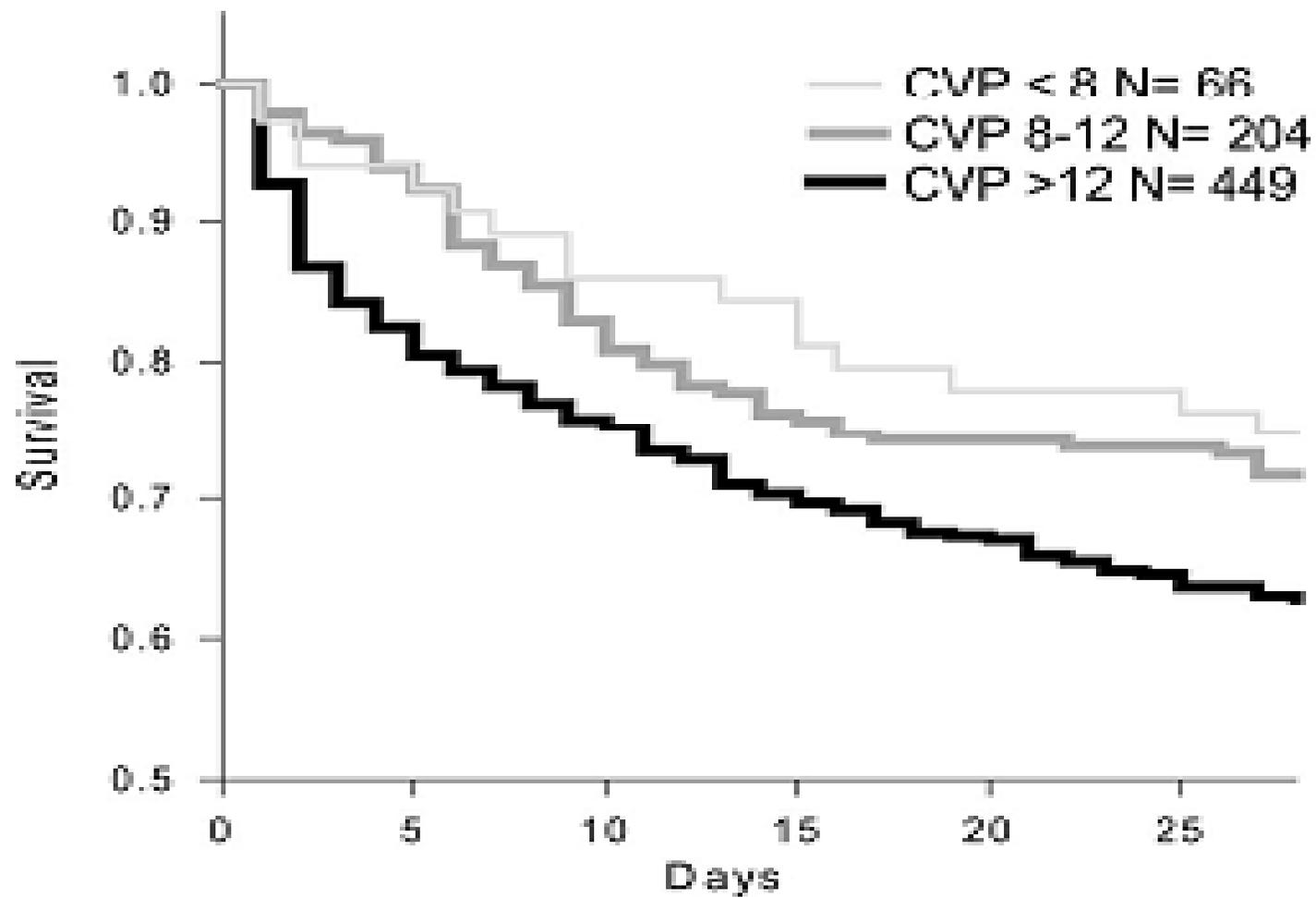
参考值： $ScvO_2 > 70\%$

液体复苏的思考

- ◆ 复苏液体的选择
- ◆ 液体复苏的评价指标
- ◆ EGDT的挑战

A

Adjusted Survival Curves CVP Groups 12 hours



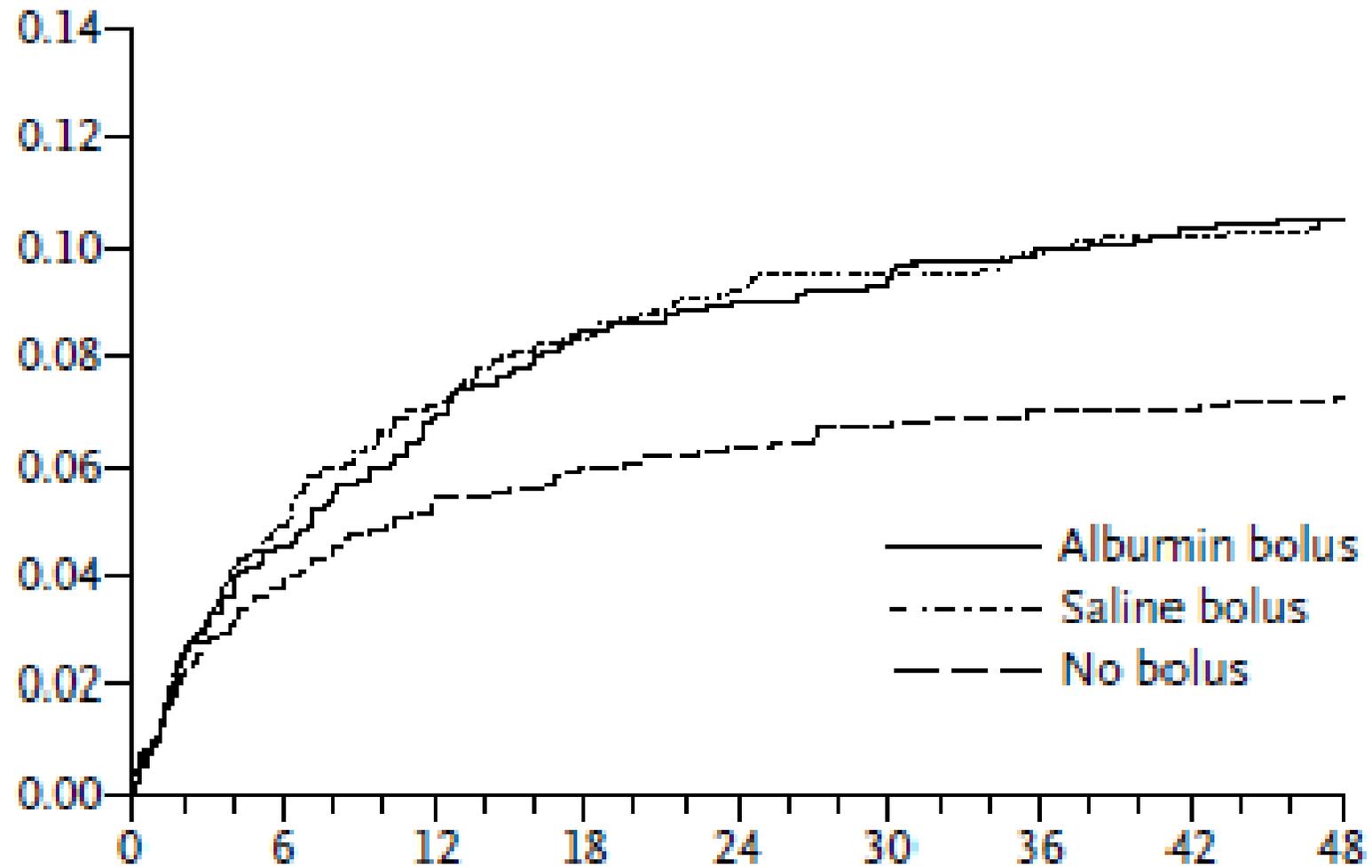
Boyd JH, et al. Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med 2011, 39(2):259-265

Table 2. Death and Other Adverse Event End Points at 48 Hours and 4 Weeks.

End Point	Albumin Bolus (N=1050)	Saline Bolus (N=1047)	No Bolus (N=1044)	Saline Bolus vs. No Bolus		Albumin Bolus vs. No Bolus		Albumin Bolus vs. Saline Bolus		Albumin and Saline Boluses vs. No Bolus	
				Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
no. (%)											
48 Hours											
Death — no. (%)	111 (10.6)	110 (10.5)	76 (7.3)	1.44 (1.09–1.90)	0.01	1.45 (1.10–1.92)	0.008	1.00 (0.78–1.29)	0.96	1.45 (1.13–1.86)	0.003
Pulmonary edema — no. (%)	14 (1.3)	6 (0.6)	6 (0.6)								
Increased intracranial pressure — no. (%)	16 (1.5)	18 (1.7)	11 (1.1)								
Severe hypotension — no. (%) ^{††}	1 (0.1)	2 (0.2)	3 (0.3)								
Allergic reaction — no. (%)	3 (0.3)	4 (0.4)	2 (0.2)								
Pulmonary edema, increased intracranial pressure, or both — no. (%) ^{††}	27 (2.6)	23 (2.2)	17 (1.6)	1.34 (0.72–2.51)	0.34	1.57 (0.87–2.88)	0.10	1.17 (0.68–2.03)	0.49	1.46 (0.85–2.53)	0.17
4 Weeks											
Death — no. (%)	128 (12.2)	126 (12.0)	91 (8.7)	1.38 (1.07–1.78)	0.01	1.40 (1.08–1.80)	0.01	1.01 (0.80–1.28)	0.91	1.39 (1.11–1.74)	0.004
Neurologic sequelae — no./total no. (%) [‡]	22/990 (2.2)	19/996 (1.9)	20/997 (2.0)	0.95 (0.51–1.77)	0.87	1.10 (0.61–2.01)	0.74	1.16 (0.63–2.14)	0.62	1.03 (0.61–1.75)	0.92
Neurologic sequelae or death — no./total no. (%) [‡]	150/990 (15.2)	145/996 (14.6)	111/997 (11.1)	1.31 (1.04–1.65)	0.02	1.36 (1.08–1.71)	0.008	1.04 (0.84–1.28)	0.71	1.33 (1.09–1.64)	0.005

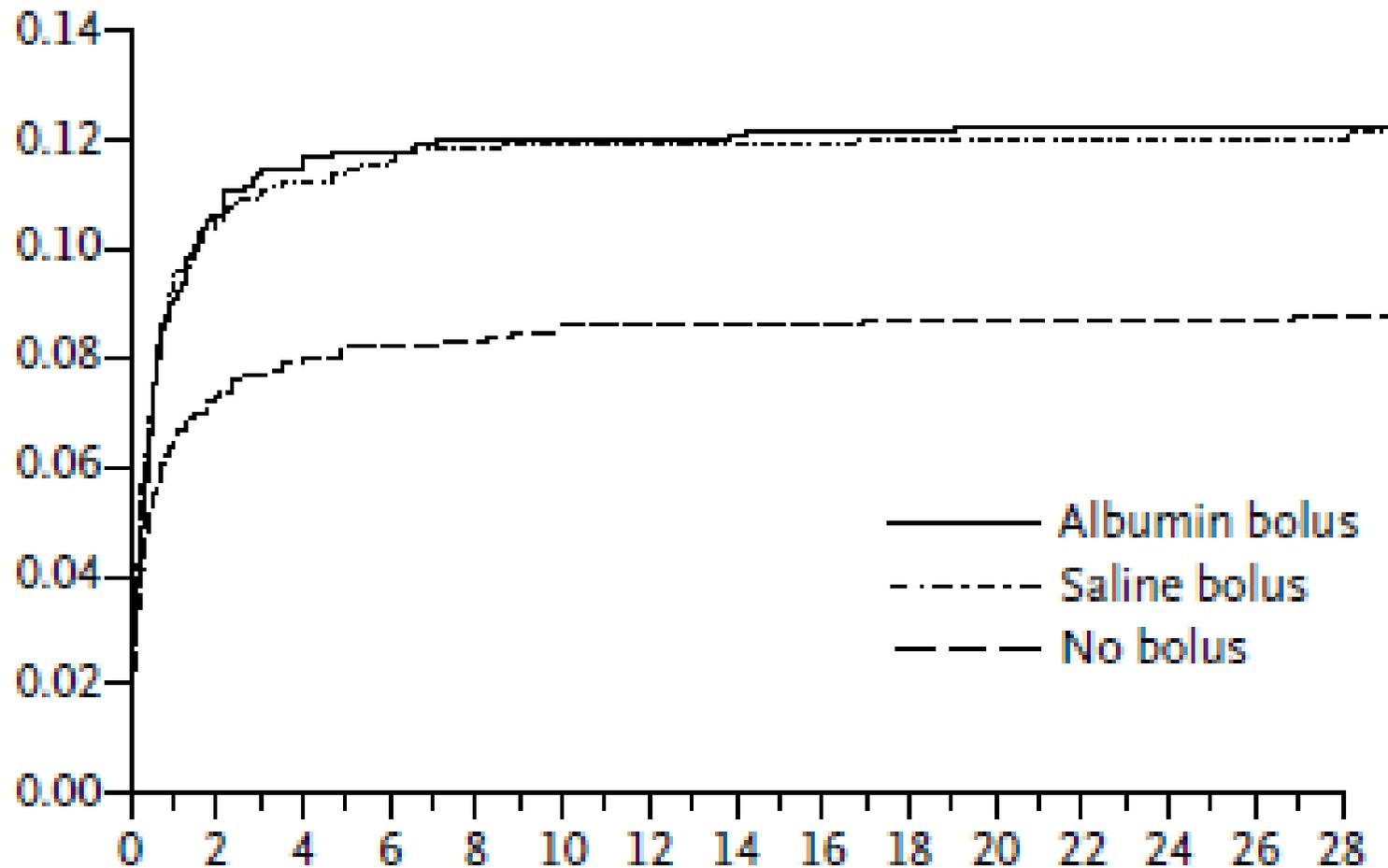
Kathryn Maitland, et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med* 2011, 364:2483-2495

A Mortality at 48 Hours



Kathryn Maitland, et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med* 2011, 364:2483-2495

B Mortality at 4 Weeks



Kathryn Maitland, et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med* 2011, 364:2483-2495

过量液体复苏的影响

- 严重脓毒症患者会出现心肌顿抑、毛细血管通透性增加
- 过量的液体复苏会加重心脏负担、增加毛细血管渗漏、阻断儿茶酚胺介导的宿主防御反应
- 过快的液体复苏可能会导致肺水肿、颅内压增高、缺血再灌注损伤等并发症

脓毒症-心肌顿抑

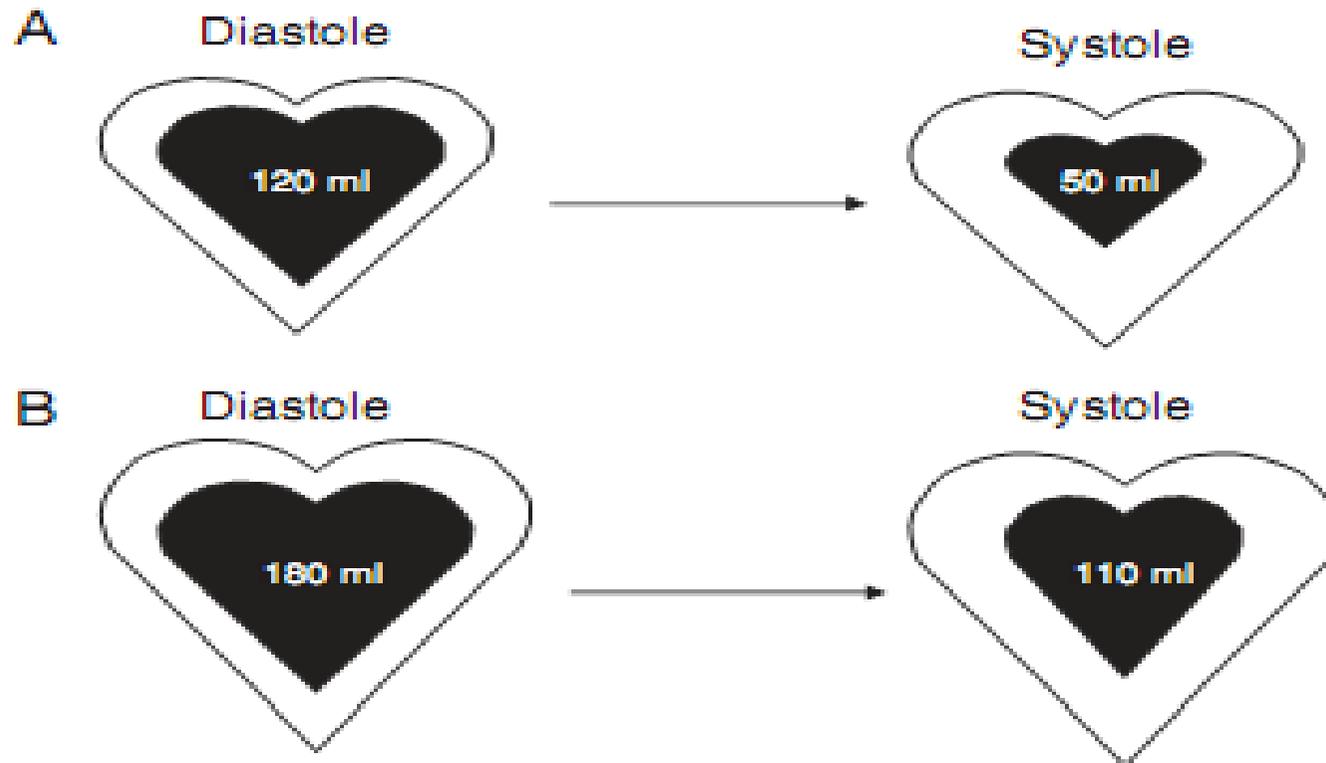


Fig 1 A decrease in EF and increased end-diastolic volume are commonly observed in septic shock. Stroke volume (SV)=LV end-diastolic volume (LVEDV)-LV end-systolic volume (LVESV). $EF=SV/LVEDV$. (A) Normal myocardium; $SV=70$ ml, $EF=(120-50)/120=0.58$. (B) Septic myocardium; $SV=70$ ml, $EF=(180-110)/180=0.39$.

关于EGDT的多中心临床研究

- **Protocolized Care for Early Septic Shock (ProCESS)**
(From Mar 2008 to Aug 2013, n=1935, US)
- **ARISE-RCT: Australasian Resuscitation In Sepsis Evaluation Randomised Control Trial**
(From Mar 2011, n=1600, Australia、New Zealand、Finland and Hong Kong)
- **ProMISe (Protocolised Management In Sepsis)**
(From Apr 2010 to Mar 2014, n=1260, UK)