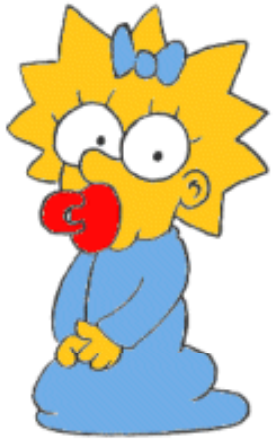
浅谈创伤与创伤性脓毒症早期治疗

解放军总医院急救医学中心

黎檀实

从一个病例说起



- XX，女，18岁，2010年07月17日10时摩托车车祸伤
- 诊断

  失血性休克

  多发骨折（左股骨干骨折 左胫腓骨开放骨折 左前臂骨折 骨盆骨折 ）

  腹腔脏器损伤？
- 当地医院处理

  Hb 56g
  K+ 2.83
  Na + 142
  CK 51468

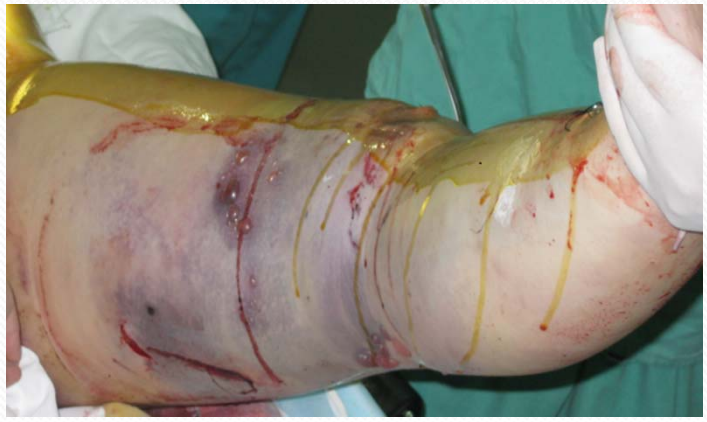
  给予 RBC220ml 血浆400ml 液体量7300ml

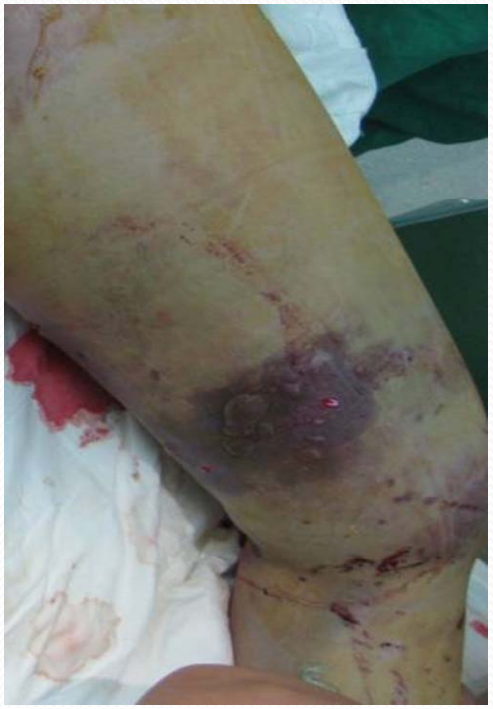
  生命体征 R25次/分 HR150 Bp 55/35

  决定转院，17日21时入解放军总医院急诊科

急诊科救治情况

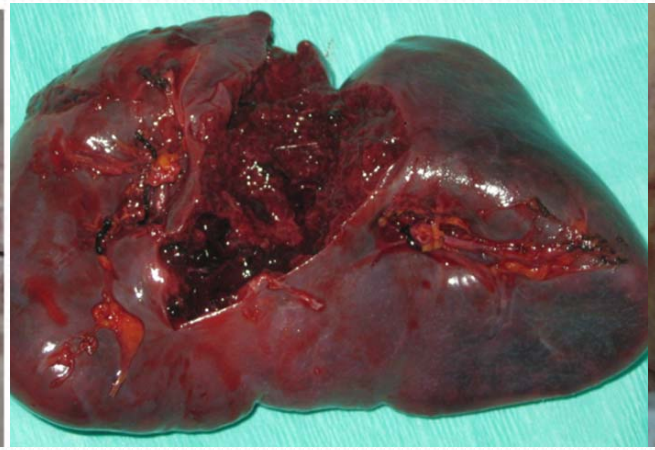
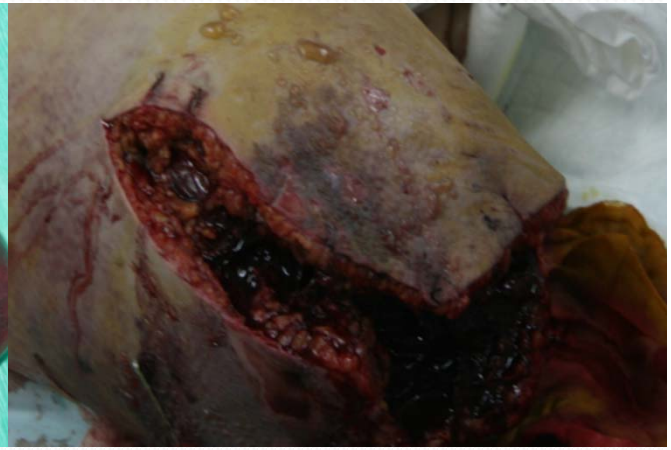
- 来诊患者处深昏迷状态，血压无，心率145次/分， SPO_2测不出，双瞳孔散大固定，腹压37cmH_2O，腹腔抽出不凝血。
- 超声示脾破裂；腹膜后巨大血肿
- 相关科室会诊认为失血休克状态，DIC无法手术
- 急诊行介入下脾动脉造影栓塞术。
- 术后腹胀继续加重，血色素持续下降。
- 车祸后约30小时决定开腹手术





第一次手术术中情况

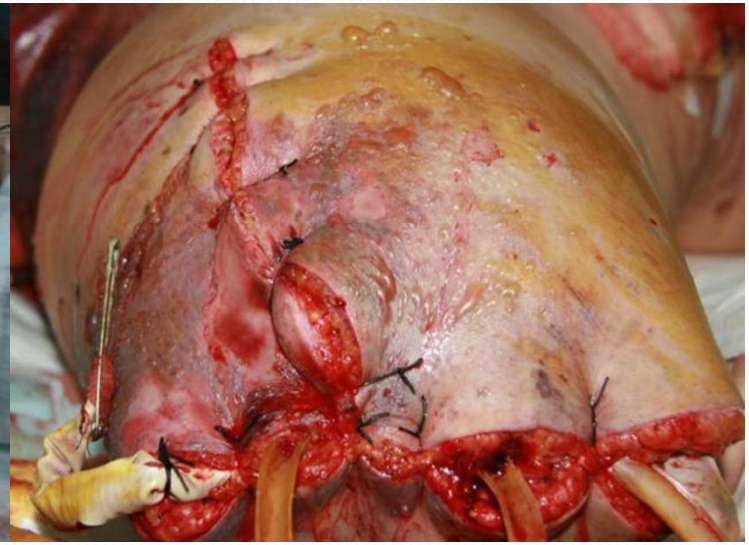
- 血性液体喷涌而出，大量暗红色不凝血及凝血块，脾脏缺血样暗红色改变，被膜可见星芒状裂口，深达脾门；腹膜后巨大血肿，累计左肾筋膜前方、肠系膜根部、左侧结肠旁沟以及脐下腹壁左下肢肌肉完全坏死，皮肤软组织广泛脱套伤；
- 左足末梢循环差，颜色苍白，肢体冰冷；
- 股动脉连续性存在，管腔血栓栓塞，肌间隙内大量血肿；
- 坏死组织有恶臭味。

术后外科重症监护病房治疗

- 综合治疗
- 抗休克治疗
- 输RBC、血浆、凝血因子等，纠正DIC
- CRRT
- 抗生素控制感染（美平 万古 米开民）

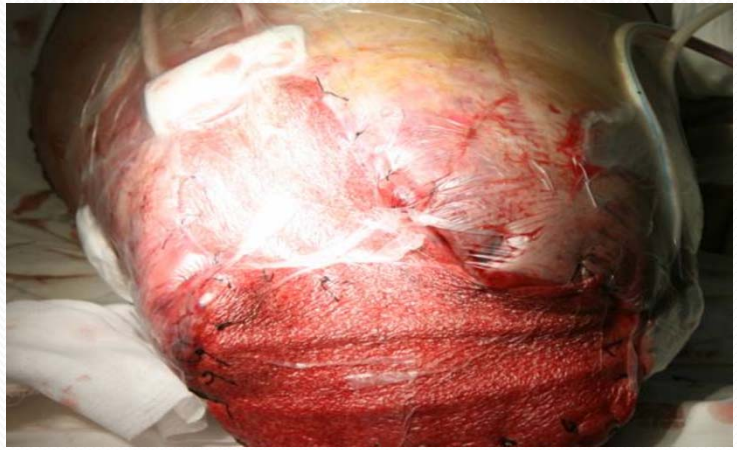




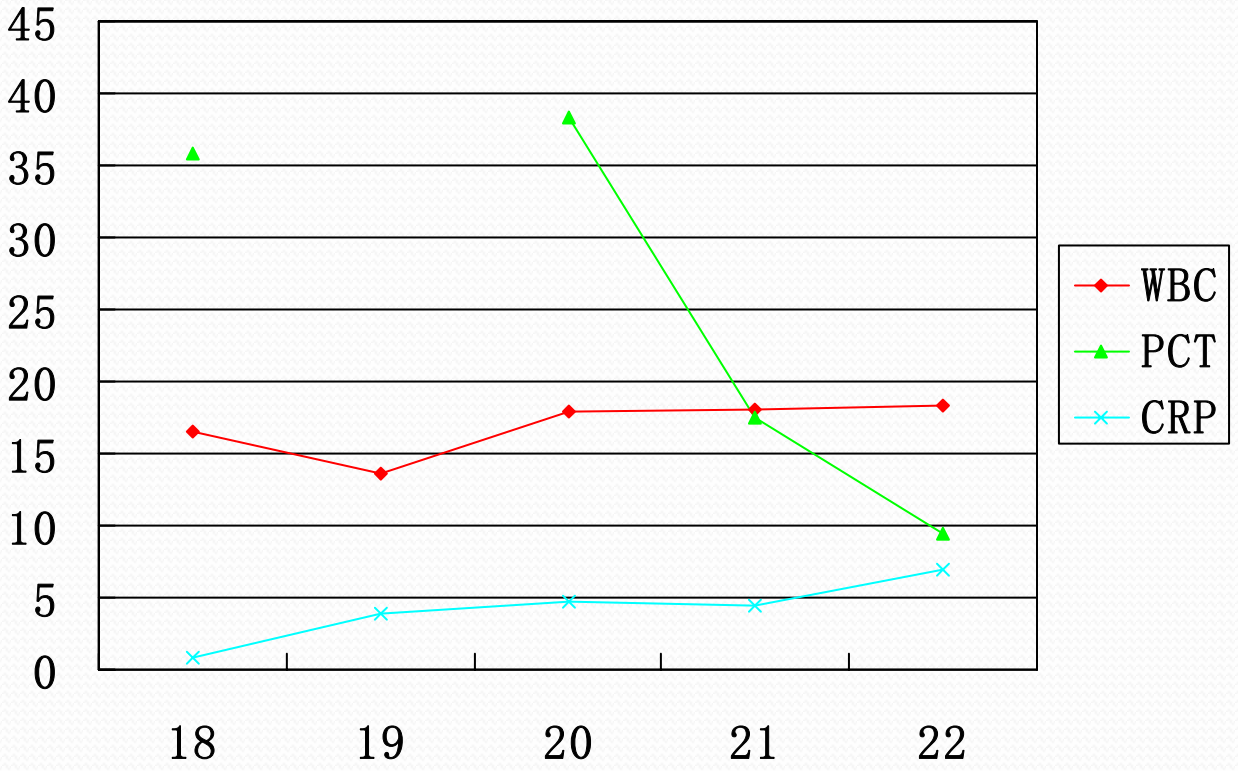
左下肢情况

- 会阴明显肿胀，大腿根部皮肤张力高，皮温降低
- 持续VSD引流
- 术中组织培养回报示产气荚膜梭菌

  卢院士等专家决定左下肢行二次手术
- 调节抗生素：加用青霉素 480wu Q6h
- 第二次手术前（7-22）

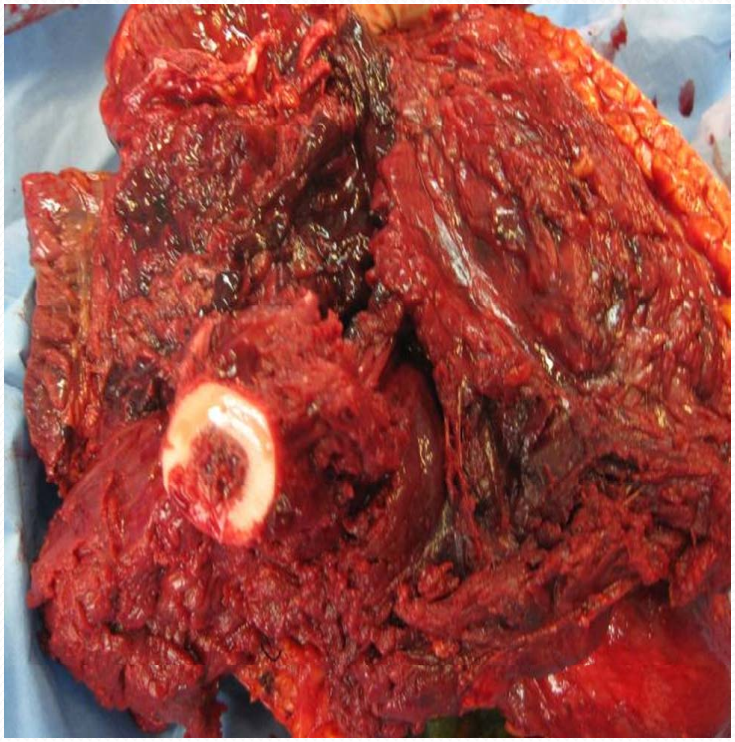


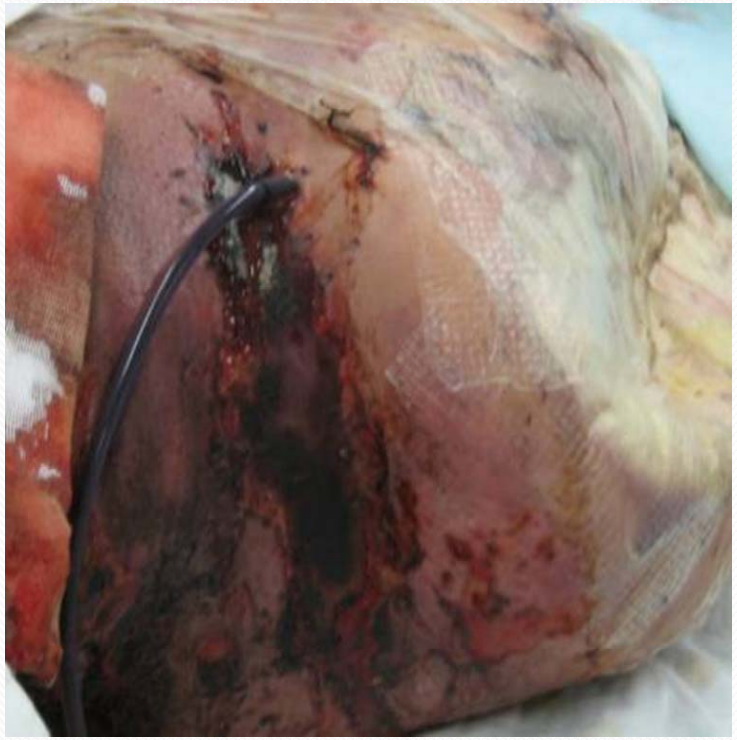
感染指标(7月18-22)



第二次手术 7-22

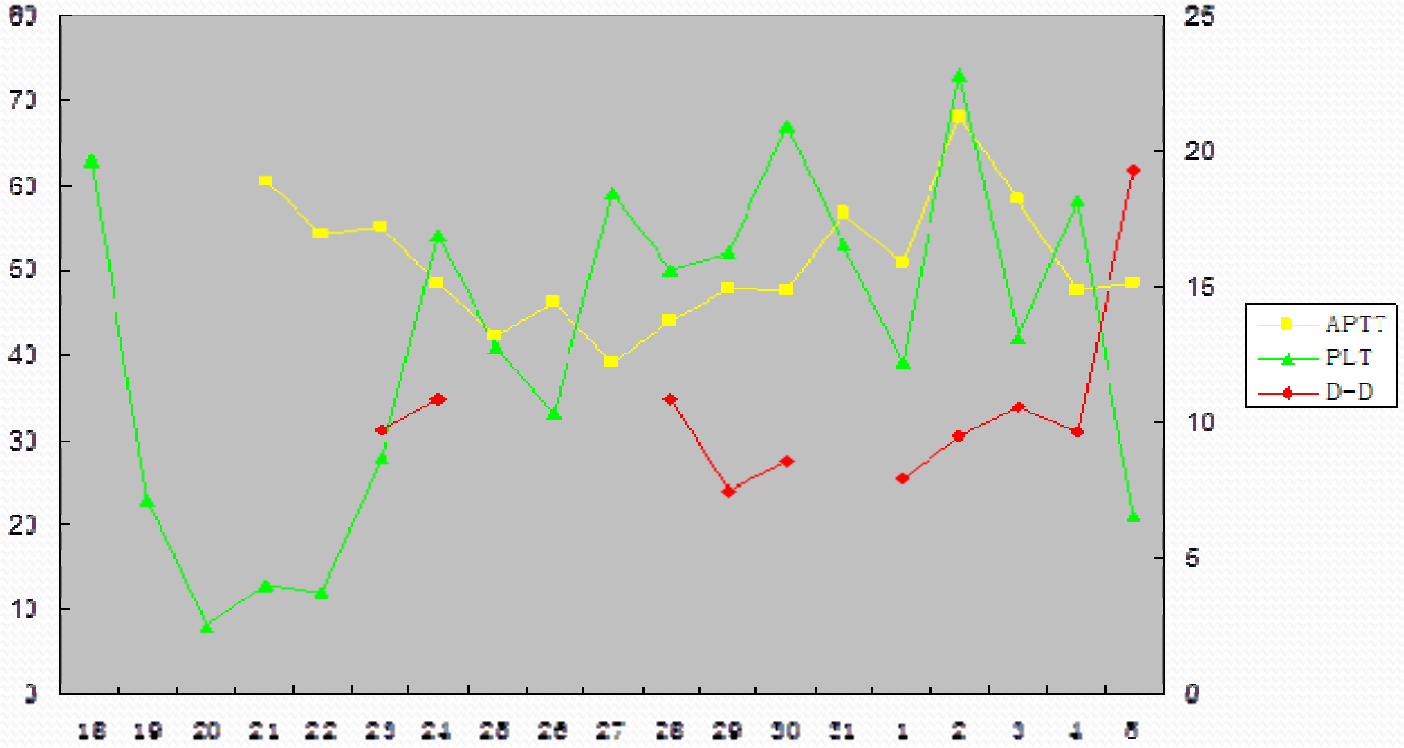
- 左下肢二次手术：小转子下截肢，残端修整 术中送培养
- 术后处理：局部处理：VSD+双氧水冲洗



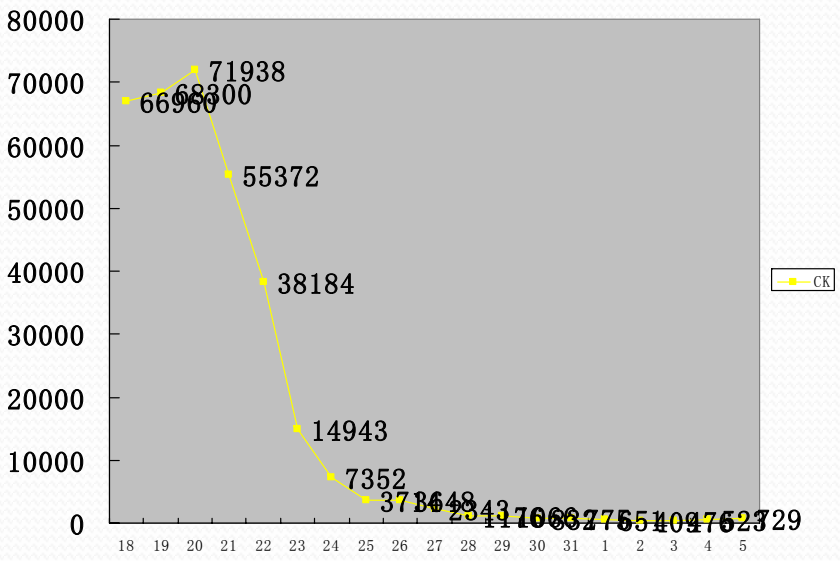


病情相对平稳期（第二次术后一周）

- 生命体征基本平稳（无升压药）
- 凝血功能趋于稳定
- 伤口引流减少



CK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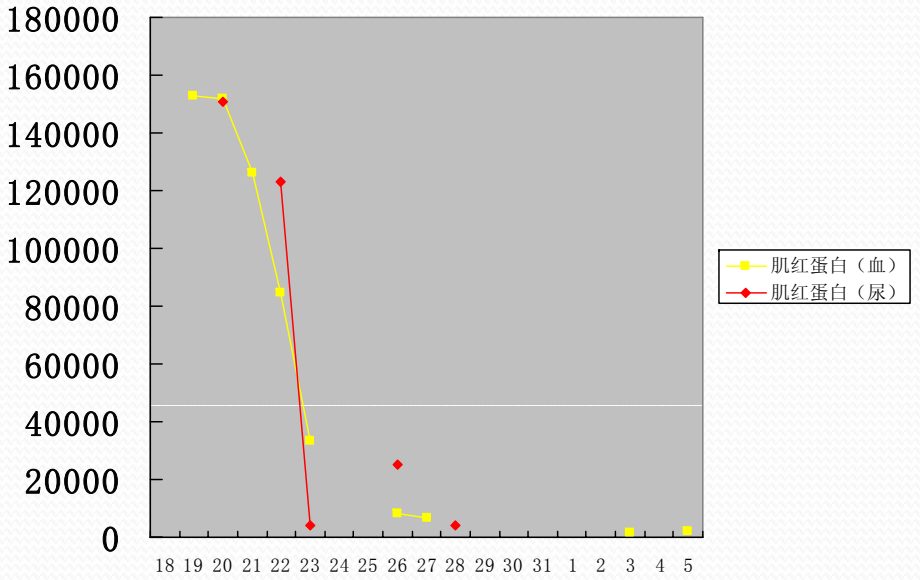
CK

肌红蛋白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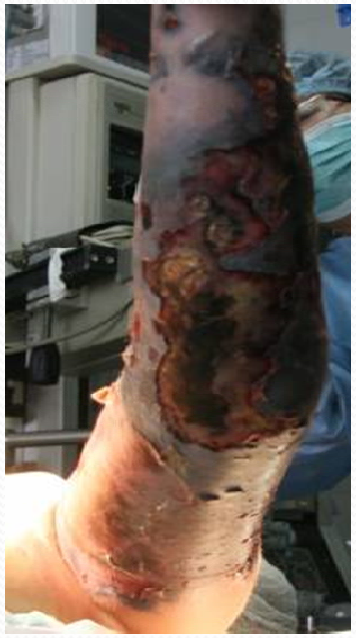
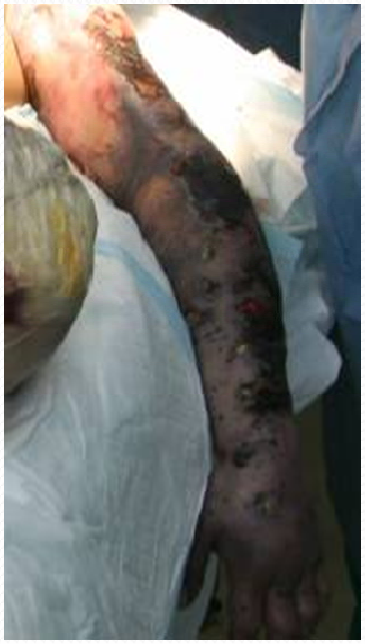
18 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2 3 4 5
肌红蛋白（血）
肌红蛋白（尿）

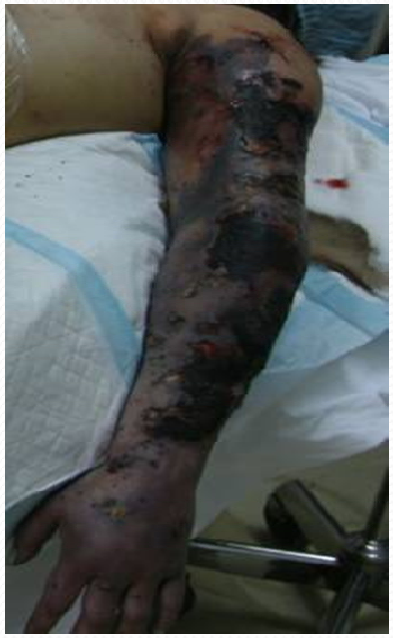
第三次手术 7-31

- 左上肢血运差，肩部皮肤发黑，末梢循环差
- 左上肢超声：皮下气肿 ，肌肉坏死可能性大 ，肱动脉、尺动脉、桡动脉无血流信号

  考虑气性坏疽感染，*决定截肢，行肩关节离断*
- 生命体征基本平稳：HR 96 BP 128/59 SPO_2 100%（Fio35%）

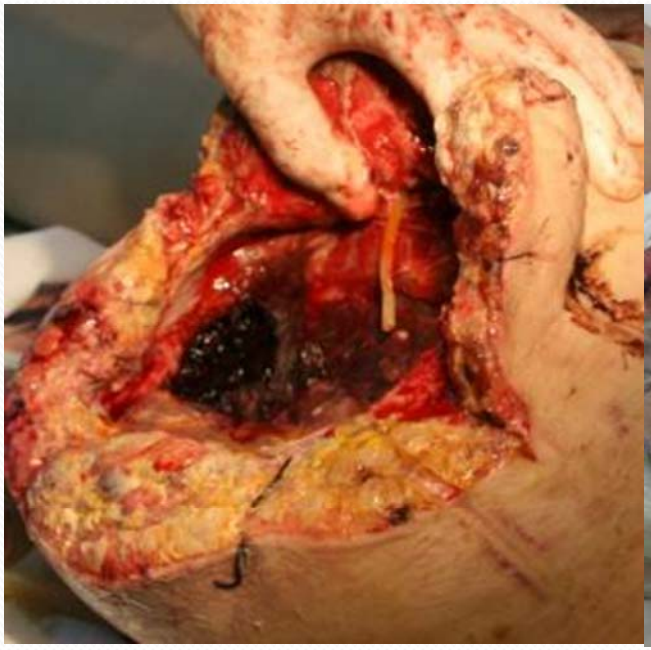


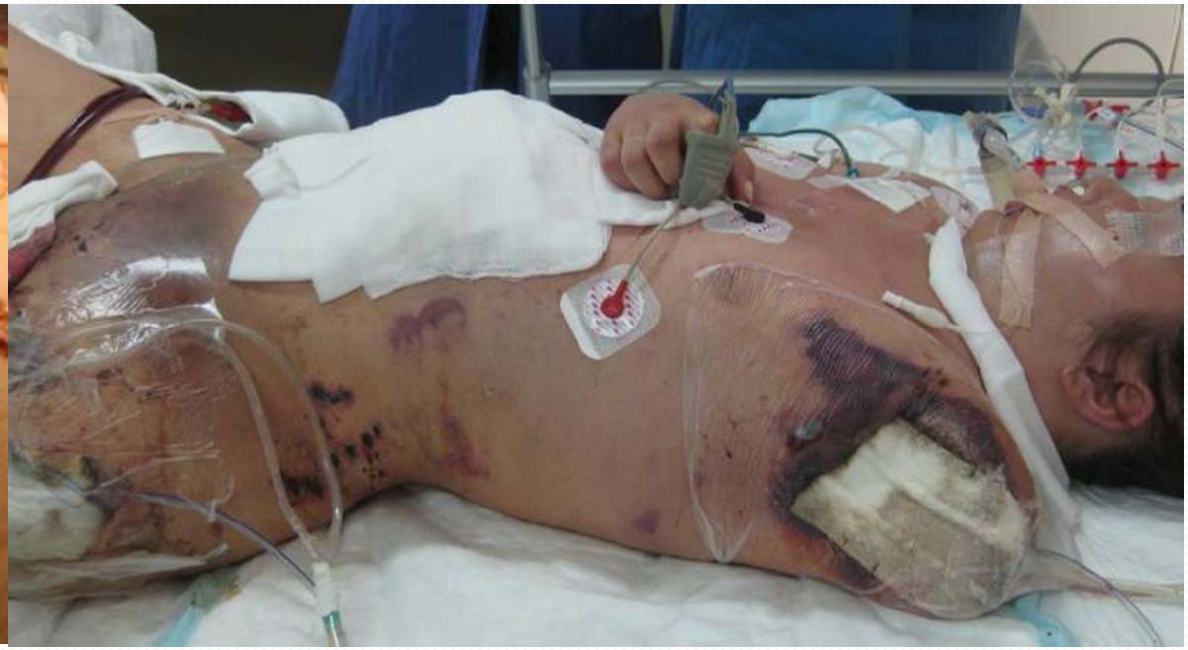




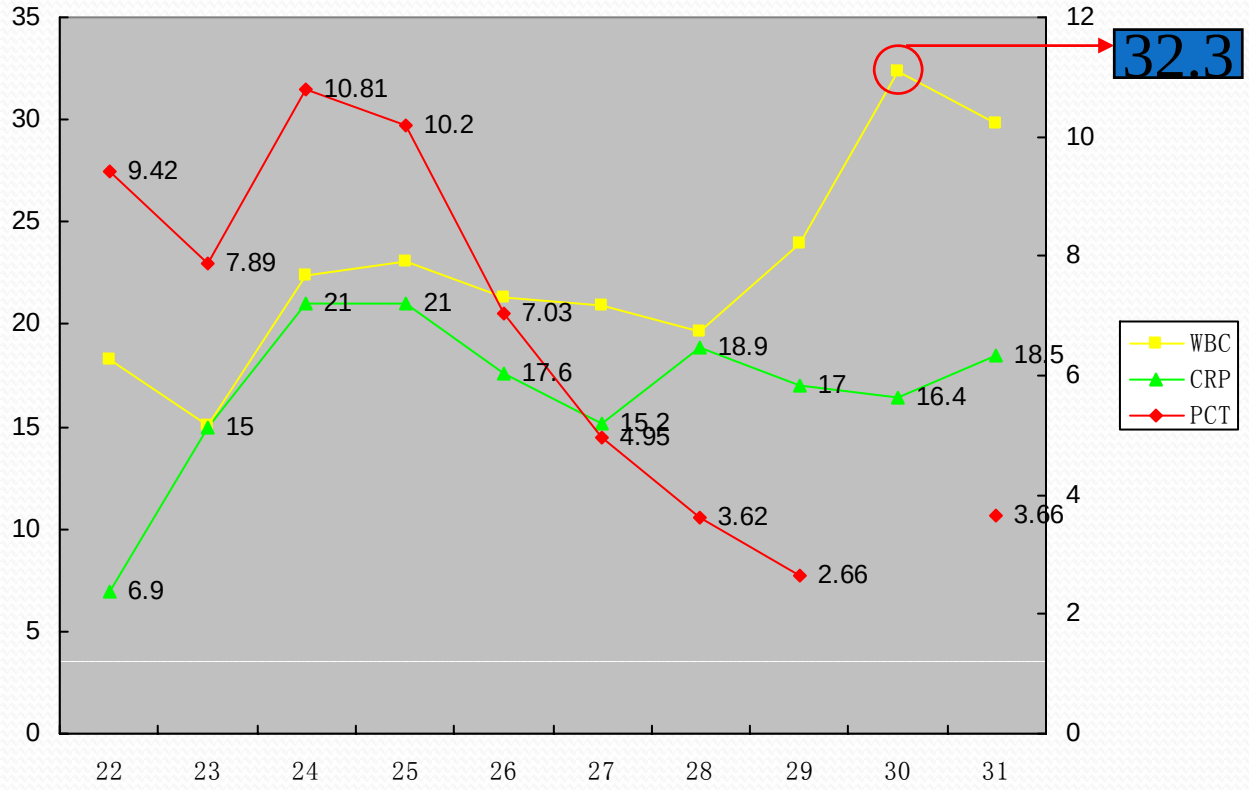
术中情况

- 发现动静脉完全闭塞、腋窝淋巴结坏死，并向近端延伸至胸壁；
- 肩关节周围肌肉大部分坏死
- 切除、冲洗，术中涂片见阳性杆菌，培养未见厌氧菌





感染指标（7月22-31）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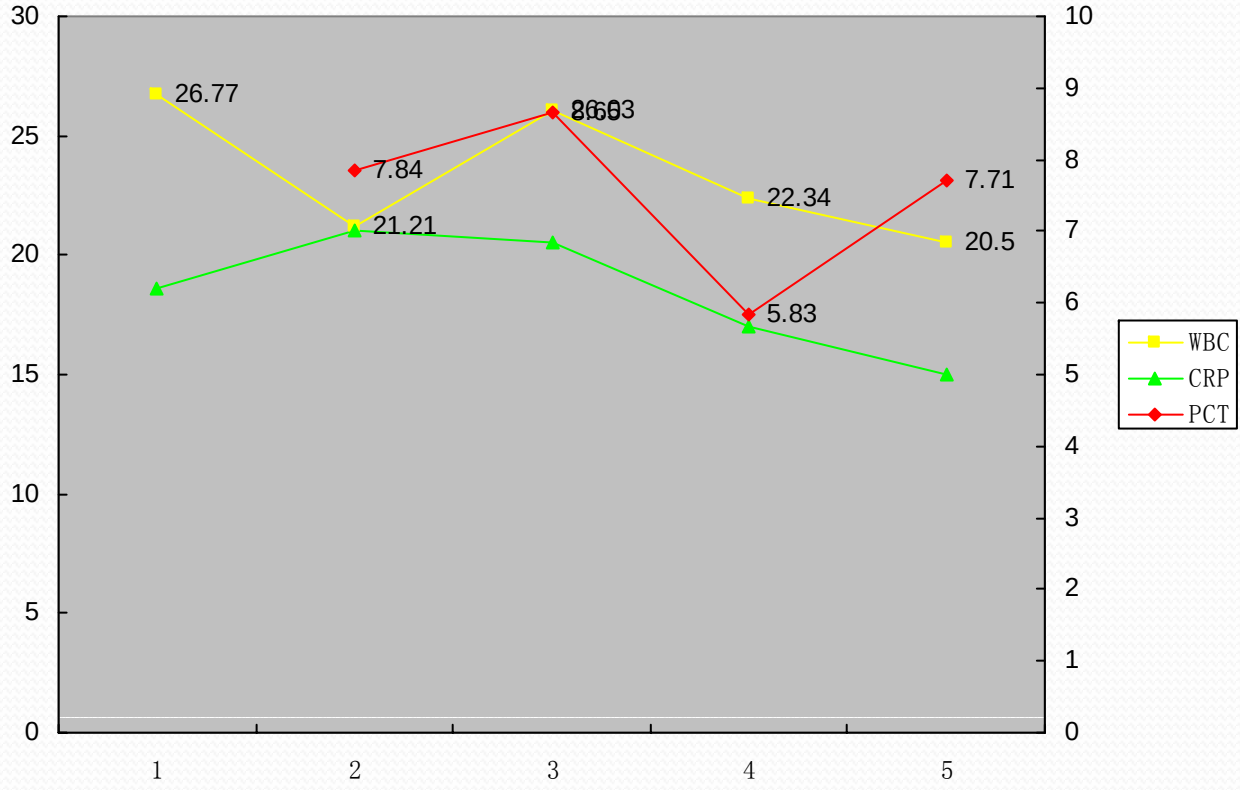
32.3
10.81
10.2
9.42
7.89
21
21
7.03
18.9
18.5
17.6
17
16.4
15
15.2
4.95
3.62
3.66
2.66
6.9
WBC
CRP
PCT

第三次术后病情演变

- 感染加重
- 氧合变差
- WBC最高3.2万
- PCT渐升高
- 8月5日死亡



Highway to Hell-Severe Sepsis！

手术时机选择是否及时？

休克、DIC 是否为手术的禁忌症？

DCS 实施的时机与方式

- **Severe Sepsis 治疗依然非常困难！**

坏死组织无法彻底清除

腹膜后巨大血肿

腹腔开放状态与患肢交叉感染

- 气性坏疽的处理

上肢感染的途径？

抗生素的应用

局部伤口的处理（开放，冲洗）

高压氧治疗？

创伤之痛




- A.J.Walt(1988)：

“如果缴税和死亡是人生逃脱不了的两件事，那么第三件事就是创伤”

“即使其他的外科疾病都能被攻克，创伤依然会存在”

Walt AJ．Foreword to the first addition of trauma[M]．Trauma．4th ed．McGrail-Hill Comp．2000：XXIX

2009年中国居民死亡构成

（卫生部2010中国卫生统计年鉴）

2009年部分市县前十

Deatl

顺位

10-1-5　2009年大城市居民主要疾病死亡率及构成

10-1-6　2009年中小城市居民主要疾病死亡率及构成

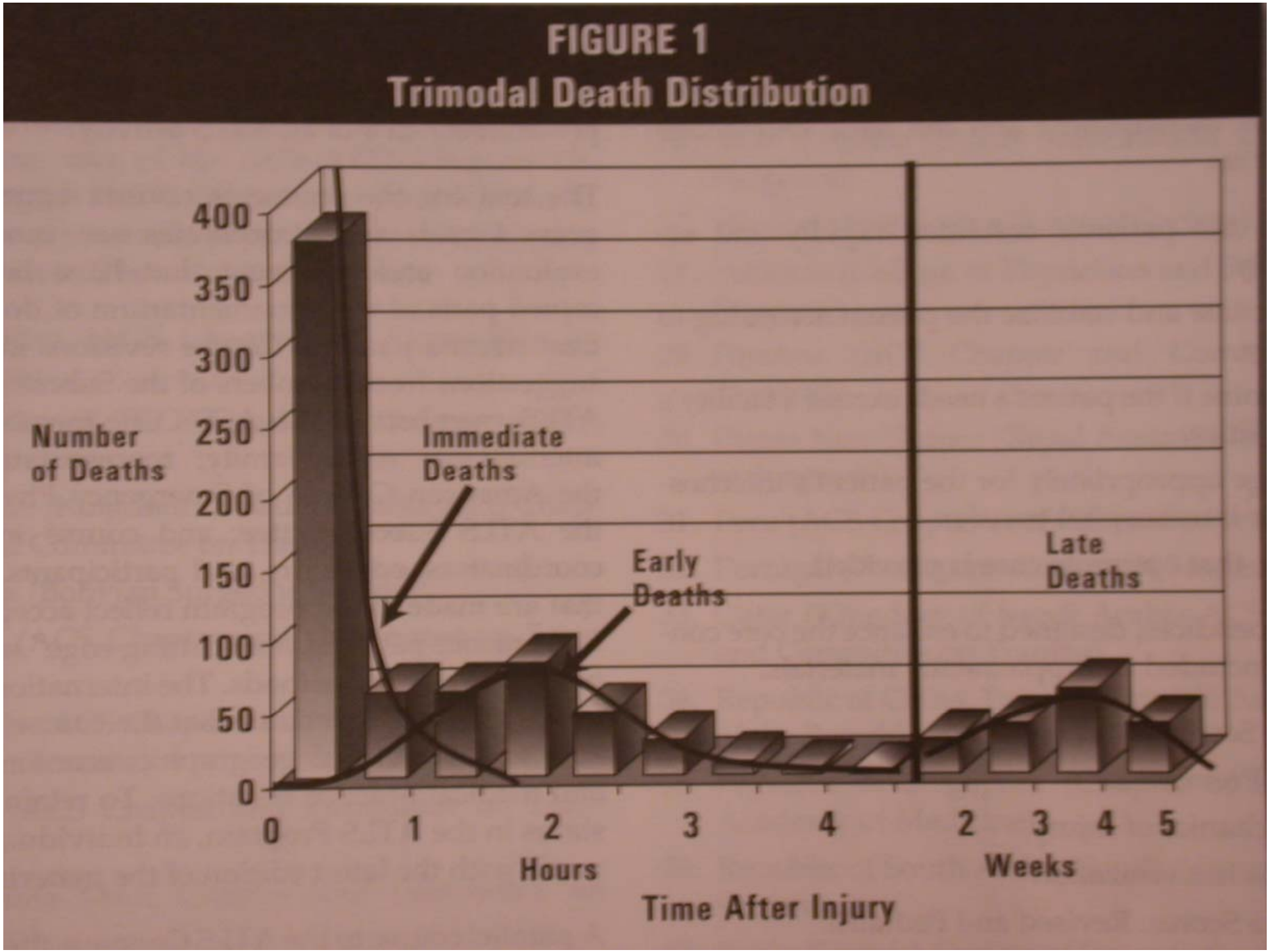
合计				男				女			
粗死亡率 1/10万	标化死亡率 1/10万	构成(%)	位次	粗死亡率 1/10万	标化死亡率 1/10万	构成(%)	位次	粗死亡率 1/10万	标化死亡率 1/10万	构成(%)	位次
5.14	4.61	0.83	11	6.07	5.54	0.91	10	4.16	3.68	0.74	12
7.31	5.57	1.19	8	9.10	7.32	1.36	8	5.42	3.95	0.97	10
0.56	0.43	0.09	17	0.62	0.50	0.09	17	0.50	0.36	0.09	18
112.57	87.33	18.30	3	139.12	112.77	20.82	2	84.62	62.81	15.12	3
6.84	5.32	1.11	10	6.08	5.09	0.91	11	7.64	5.57	1.37	8
0.86	0.75	0.14	16	0.82	0.76	0.12	16	0.90	0.74	0.16	17
4.14	2.80	0.67	12	3.93	3.07	0.59	12	4.36	2.48	0.78	11
2.85	2.46	0.46	15	3.07	2.83	0.46	13	2.62	2.09	0.47	15
73.43	49.40	11.94	4	72.03	55.14	10.78	5	74.90	44.48	13.39	4
115.20	78.18	18.73	2	124.05	95.37	18.57	3	105.89	63.02	18.93	2
142.16	98.97	23.11	1	143.40	114.44	21.46	1	140.86	85.85	25.18	1
23.89	18.99	3.88	6	28.06	23.57	4.20	6	19.50	14.49	3.48	6
9.27	7.06	1.51	7	10.33	8.32	1.55	7	8.15	5.99	1.46	7
0.56	0.50	0.09	18					1.16	1.03	0.21	18
2.92	4.71	0.47	13	2.98	4.72	0.45	14	2.85	4.69	0.51	14
6.99	14.43	1.14	9	7.04	14.11	1.05	9	6.93	14.79	1.24	9
2.89	1.98	0.47	14	2.58	2.05	0.39	15	3.22	1.88	0.58	13
64.89	57.16	10.55	5	78.66	71.18	11.77	4	50.40	43.47	9.01	5

十种死因合计　Total　93.52　十种死因合计　Total　94.78

10-5-3　2000年农村居民主要疾病死亡率及构成

疾病名称	合计				男				女			
	粗死亡率 1/10万	标化死亡率 1/10万	构成(%)	位次	粗死亡率 1/10万	标化死亡率 1/10万	构成(%)	位次	粗死亡率 1/10万	标化死亡率 1/10万	构成(%)	位次
传染病(不含肺结核)	5.14	4.61	0.83	11	6.07	5.54	0.91	10	4.16	3.68	0.74	12
肺结核	7.31	5.57	1.19	8	9.10	7.32	1.36	8	5.42	3.95	0.97	10
寄生虫病	0.56	0.43	0.09	17	0.62	0.50	0.09	17	0.50	0.36	0.09	18
恶性肿瘤	112.57	87.33	18.30	3	139.12	112.77	20.82	2	84.62	62.81	15.12	3
内分泌营养和代谢及免疫疾病	6.84	5.32	1.11	10	6.08	5.09	0.91	11	7.64	5.57	1.37	8
血液和造血器官疾病	0.86	0.75	0.14	16	0.82	0.76	0.12	16	0.90	0.74	0.16	17
精神病	4.14	2.80	0.67	12	3.93	3.07	0.59	12	4.36	2.48	0.78	11
神经系病	2.85	2.46	0.46	15	3.07	2.83	0.46	13	2.62	2.09	0.47	15
心脏病	73.43	49.40	11.94	4	72.03	55.14	10.78	5	74.90	44.48	13.39	4
脑血管病	115.20	78.18	18.73	2	124.05	95.37	18.57	3	105.89	63.02	18.93	2
呼吸系病	142.16	98.97	23.11	1	143.40	114.44	21.46	1	140.86	85.85	25.18	1
消化系病	23.89	18.99	3.88	6	28.06	23.57	4.20	6	19.50	14.49	3.48	6
泌尿、生殖系病	9.27	7.06	1.51	7	10.33	8.32	1.55	7	8.15	5.99	1.46	7
妊娠分娩产褥期并发症	0.56	0.50	0.09	18					1.16	1.03	0.21	18
先天异常	2.92	4.71	0.47	13	2.98	4.72	0.45	14	2.85	4.69	0.51	14
新生儿病	6.99	14.43	1.14	9	7.04	14.11	1.05	9	6.93	14.79	1.24	9
其他疾病	2.89	1.98	0.47	14	2.58	2.05	0.39	15	3.22	1.88	0.58	13
损伤和中毒	64.89	57.16	10.55	5	78.66	71.18	11.77	4	50.40	43.47	9.01	5

FIGURE 1
Trimodal Death Distribution



Damage control resuscitation (DCR) is a novel concept

Surgery does not follow resuscitation, it is a part of resuscitation, and DCS is a component of DCR

T J Hodgetts .et al: Damage control resuscitation
J R Army Med. Corps. 153(4):299-300

DCR理念：手术并非在复苏之后 而是复苏的一部分 DCS是DCR的组成部分

Epidemiology of sepsis in patients with traumatic injury

Table 2. Comparison of septic and nonseptic patients on demographic, clinical, and trauma-related measures

Variable	No Sepsis	Sepsis	*p*
No. (%)	29,697 (98)	606 (2)	
Gender, %			
Male	98	2	<.001
Female	99	1	
Age, mean ± SD	47.1 ± 21.7	48.8 ± 21.1	.059
ISS, mean ± SD	12.9 ± 11.6	28.1 ± 14.2	<0.001
GCS, mean ± SD	13.2 ± 3.8	10.0 ± 5.1	<.0001
SBP, mean ± SD	134 ± 37	124 ± 39	<0.001
RR, mean ± SD	18.5 ± 7.3	15.9 ± 11.2	<0.001
RTS, mean ± SD	7.2 ± 1.8	6.0 ± 2.1	<0.001
History of cardiac disease, n (%)	7,129 (24)	169 (28)	.027
History of diabetes, n (%)	2,200 (7)	55 (11)	.001
History of immune deficiency, n (%)	391 (1)	17 (3)	.002

ISS, Injury Severity Score; GCS, Glasgow Coma Scale; SBP, admission systolic blood pressure; RR, admission respiratory rate; RTS, Revised Trauma Score.

Osborn TM，Tracy JK，Dunne JR，et al．Epidemiolog of sepsis in patients with traumatic injury[J]．Cr Care Med，2004，32（11）：2234-2240

Comparison of septic and nonseptic patients for trauma-related outcome measures

Variable	Total Sample	No Sepsis	Sepsis	*p*
No. (%)	30,303	29,697 (98)	606 (2)	
ICU admission, %	41	40	94	<.001
ICU days, mean ± SD	2.1 ± 5.9	4.7 ± 7.4	21.8 ± 22.0	<.001
Hospital days, mean ± SD	7.3 ± 9.5	7.0 ± 8.7	34.1 ± 26.6	<.001
Mortality, %	7.95	7.6	23.1	<.001

Osborn TM，Tracy JK，Dunne JR，et al．Epidemiolog of sepsis in patients with traumatic injury[J]. Cr Care Med，2004，32（11）：2234-2240

Clinical characteristics of each Injury Severity Score (ISS) group

Variable	Mild Injury ISS <15	Moderate Injury ISS 15–29	Severe Injury ISS ≥30	*p* Value
No. (%)	20,511 (67.7)	7,169 (23.7)	2,623 (8.7)	
Age, yrs, mean ± SD	48.0 ± 21.8	47.0 ± 21.6	41.3 ± 20.0	≤.001[a]
Injury Severity Score, mean ± SD	6.9 ± 3.8	21.5 ± 4.3	43.0 ± 13.4	≤.001[a]
Revised Trauma Score, mean ± SD	7.6 ± 1.0	6.7 ± 2.1	4.7 ± 2.9	≤.001[a]
Respiratory rate, mean ± SD	19.6 ± 5.2	17.5 ± 9.2	11.7 ± 11.7	≤.001[a]
Admission SBP, mean ± SD	138.7 ± 28.0	131.3 ± 41.0	106.1 ± 54.5	≤.001[a]
ICU LOS, days, mean ± SD	2.7 ± 4.7	5.8 ± 8.4	10.4 ± 13.0	<.001[a]
Hospital LOS, days, mean ± SD	5.5 ± 5.8	10.2 ± 11.7	13.2 ± 17.7	<.001[a]
Sepsis, %	19	42	39	<.001[b]
Mortality, n (%)	442 (2.2)	1020 (14.2)	947 (36.1)	≤.001[b]

Sepsis: A Complex Clinical Challenge

Infection/ Trauma → SIRS → Sepsis → **Severe Sepsis**

- **High mortality rate (35%-45%)**
- **Heterogeneous patient population**
- **Unpredictable disease progression**
- **Unclear etiology and pathogenesis**

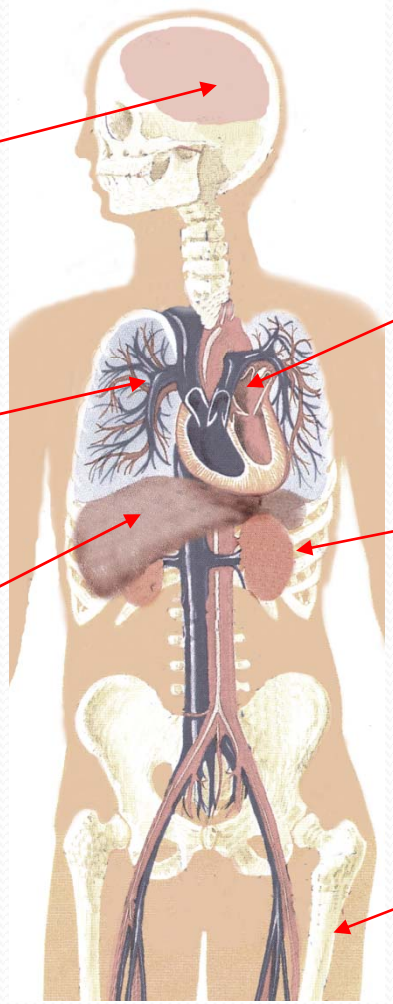
Wheeler and Bernard. *N Engl J Med*. 1999;340:207.

Identifying Acute Organ Dysfunction as a Marker of Severe Sepsis

Altered
Consciousness
Confusion
Psychosis

Tachypnea
PaO_2 <70 mm Hg
SaO_2 <90%
PaO_2/FiO_2 ≤300

Jaundice
↑ Enzymes
↓ Albumin
↑ PT

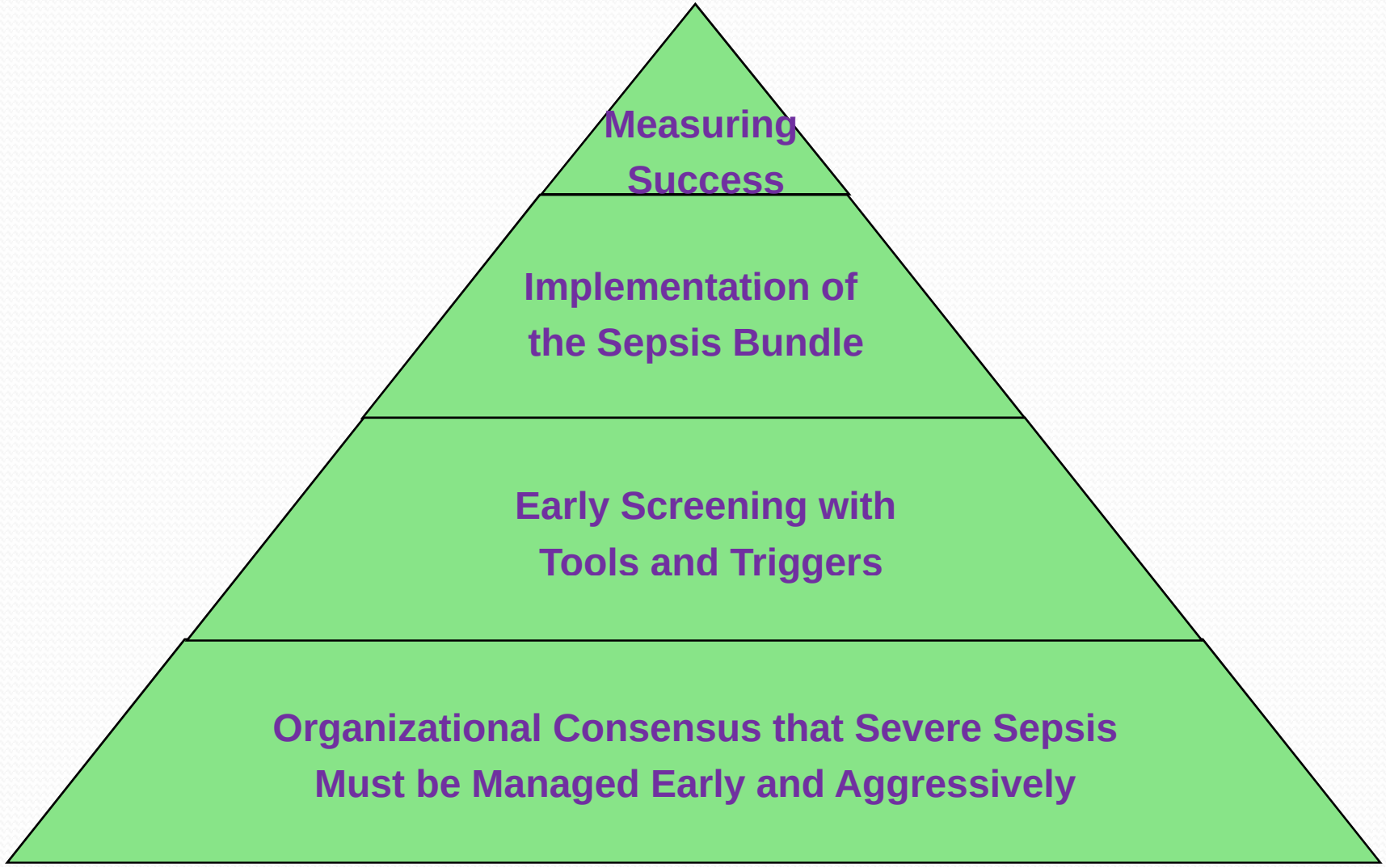


Tachycardia
Hypotension
↑ CVP
↑ PAOP

Oliguria
Anuria
↑ Creatinine

↓ Platelets
↑ PT/APTT
↓ Protein C
↑ D-dimer

4-Tier Process for Severe Sepsis Program Implementation



Early Interventions in Medicine

- AMI – "Time is Muscle"
  - ACC/AHA guidelines for STEMI
    - Door-to-needle time for initiation of fibrinolytic therapy should be achieved within 30 minutes
    - Door-to-balloon (or medical contact–to-balloon) time for PCI can be kept under 90 minutes.
- Stroke – "Time is Brain"
  - ASA
    - IV rtPA is strongly recommended within 3 hours of onset of ischemic stroke (grade A).
- Trauma
  - Golden Hour – …the lives of severely injured people could be saved if treated by trauma specialists

Severe Sepsis Bundles:

Sepsis Resuscitation Bundle

(To be accomplished as soon as possible and scored over first 6 hours):

1. Serum lactate measured.
2. Blood cultures obtained prior to antibiotic administration.
3. From the time of presentation, broad-spectrum antibiotics administered within 3 hours for ED admissions and 1 hour for non-ED ICU admissions.
4. In the event of hypotension and/or lactate > 4 mmol/L (36 mg/dl): a) Deliver an initial minimum of 20 ml/kg of crystalloid (or colloid equivalent). b) Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) > 65 mm Hg.
5. In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate > 4 mmol/L (36 mg/dl):
a) Achieve central venous pressure (CVP) of > 8 mm Hg.
b) Achieve central venous oxygen saturation ($ScvO_2$) of > 70%.*

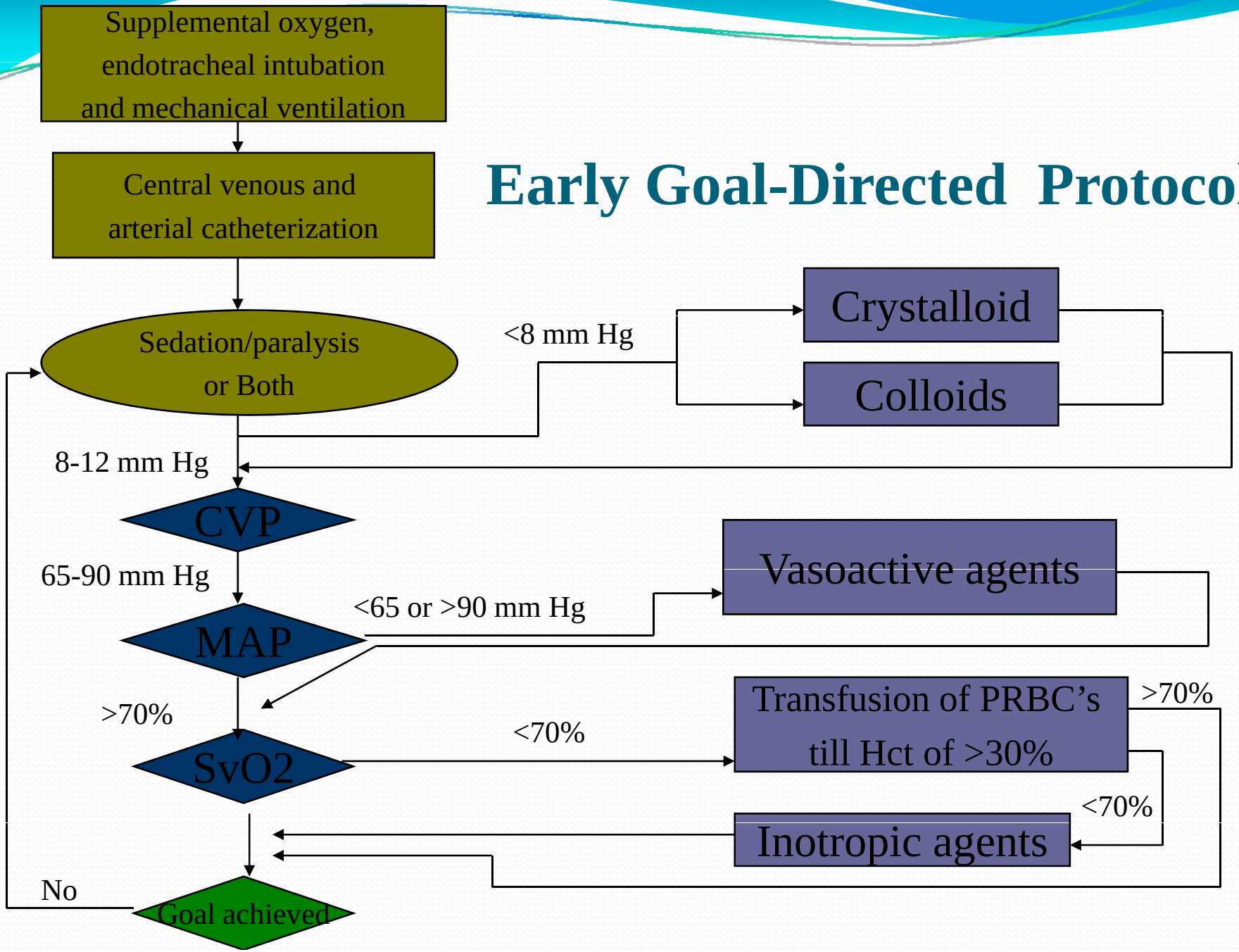
Sepsis Management Bundle

(To be accomplished as soon as possible and scored over first 24 hours):

1 Low-dose steroids administered for septic shock in accordance with a standardized hospital policy.
2 Drotrecogin alfa (activated) administered in accordance with a standardized hospital policy.
3 Glucose control maintained > lower limit of normal, but < 150 mg/dl (8.3 mmol/L).
4 Inspiratory plateau pressures maintained < 30 cm H_2O for mechanically ventilated patients.

*Achieving a mixed venous oxygen saturation (SvO_2) of 65% is an acceptable alternative.

Early Goal-Directed Protocol



Rivers NEJM 2001;345:1368

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

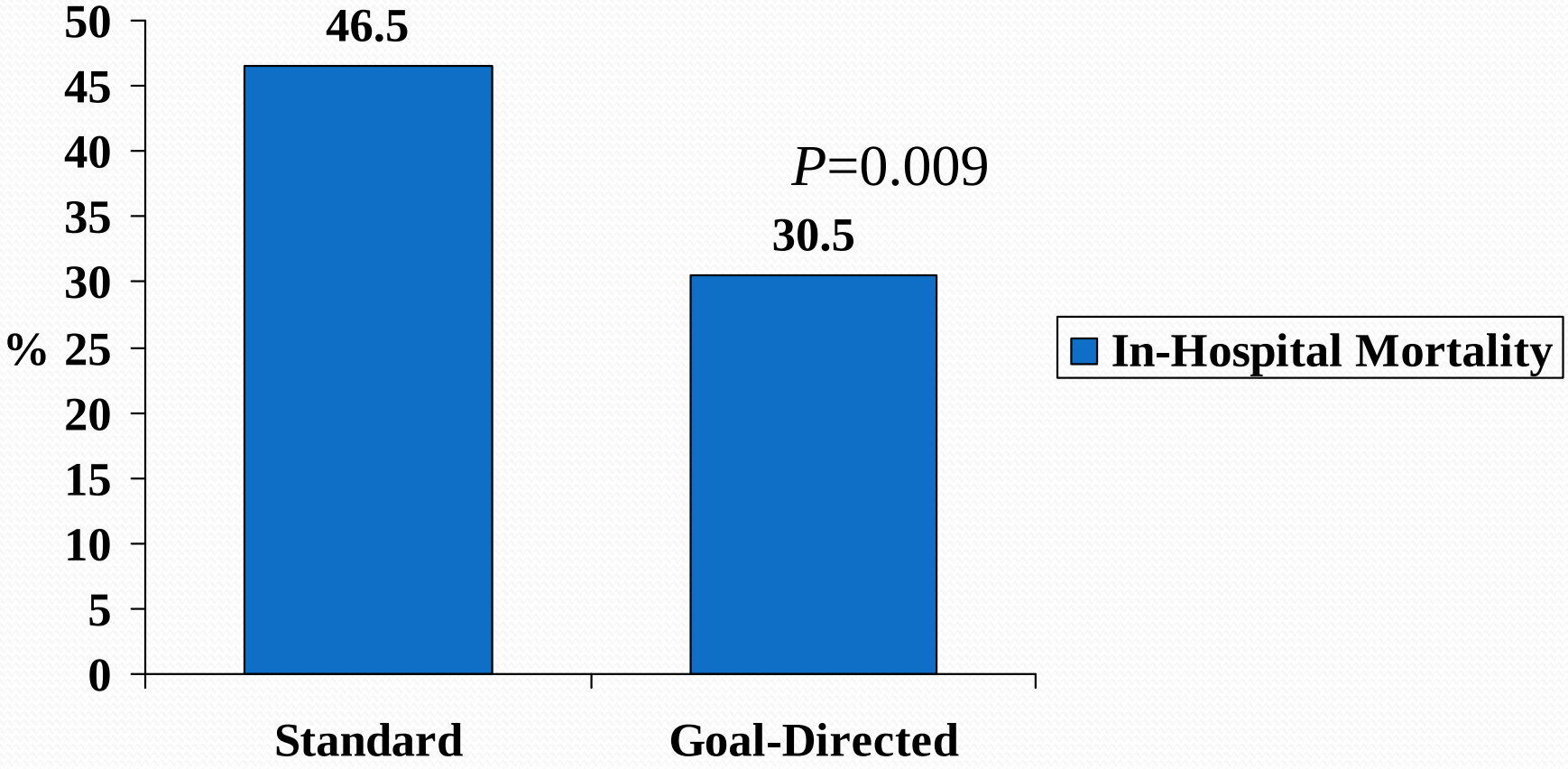
VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	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.

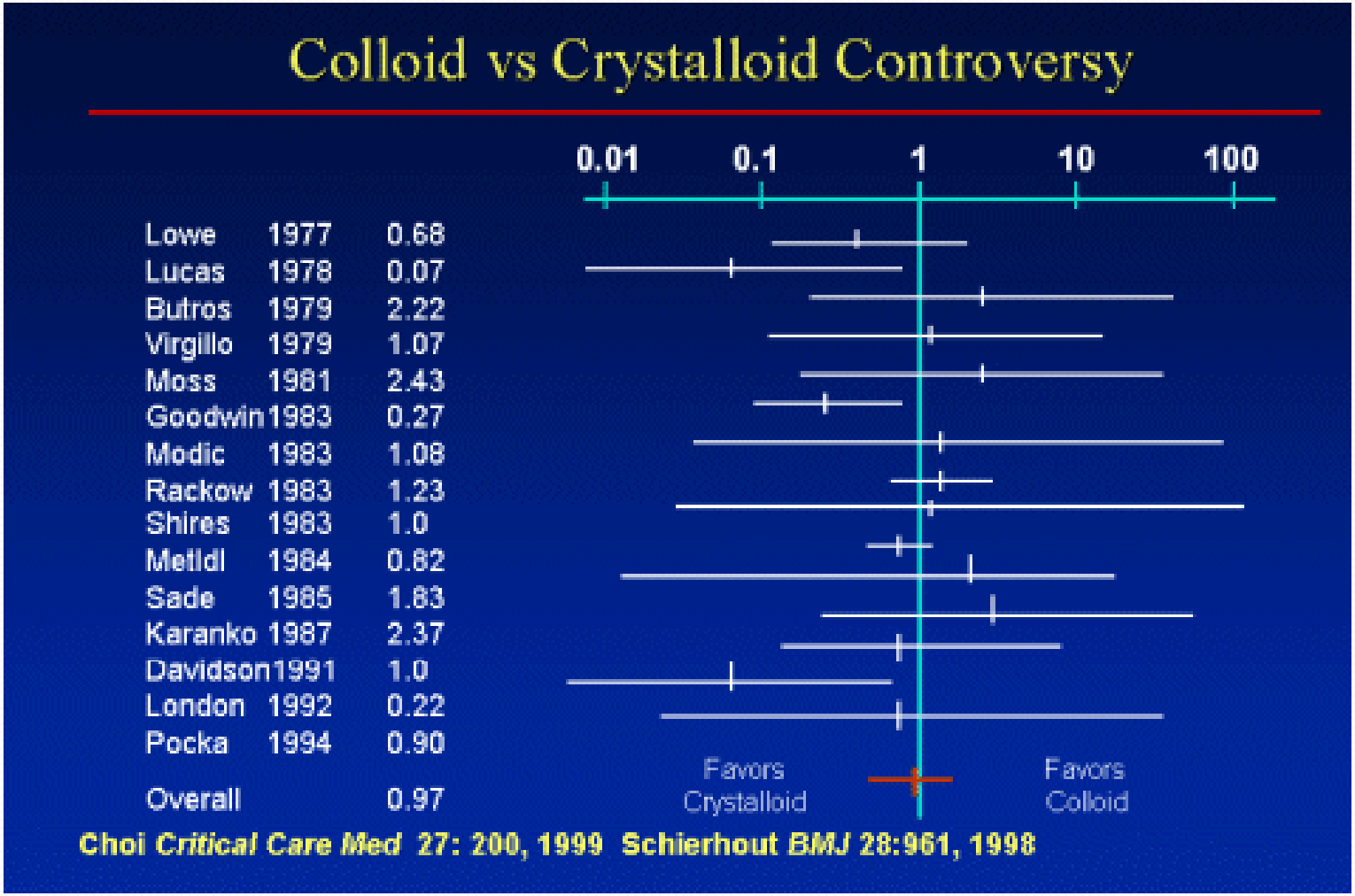
‡The denominators indicate the numbers of patients in each group who completed the initial six-hour study period.

Goal-Directed Protocol

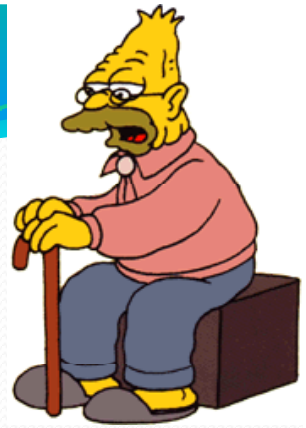


Rivers E, et al. *N Eng J Med* 2001;345:1366

Fluid Resuscitation



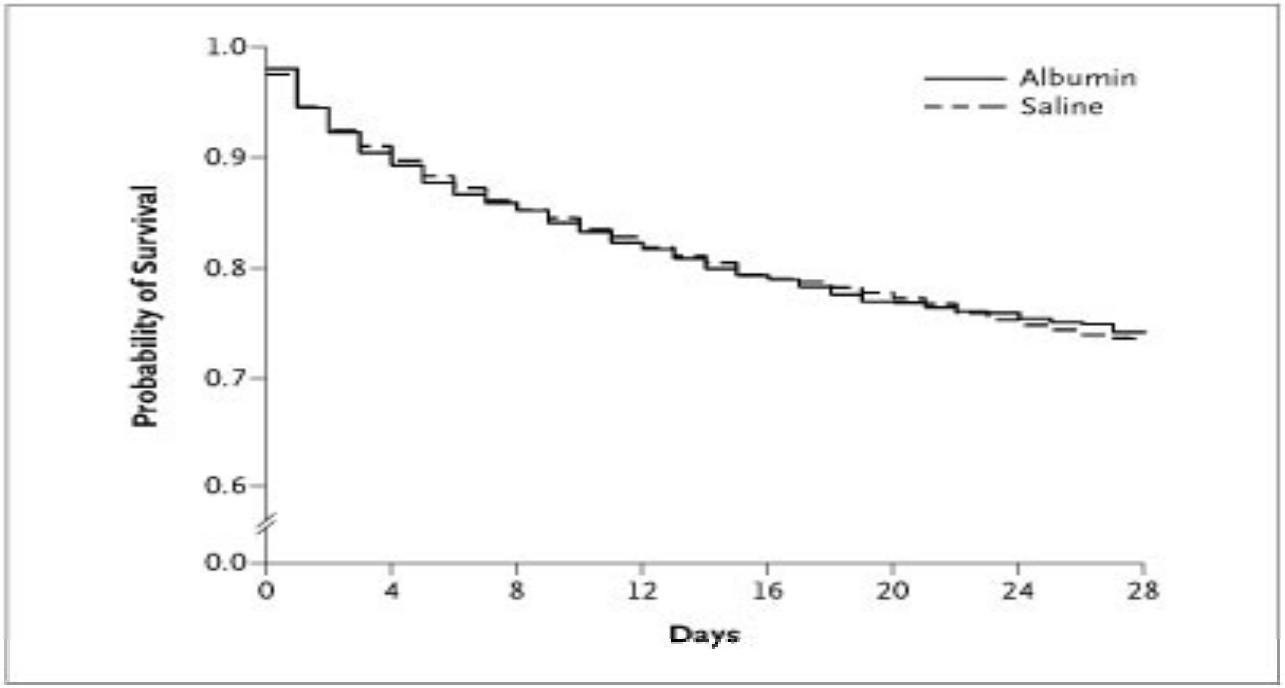
EGDT：不同液体复苏效果



- 选用晶体液、胶体液之争主要围绕于**血浆胶体渗透压**
- 如果能够维持较低水平充盈压力，晶体液或胶体液对肺水肿形成无明显差别，因罹患心室功能障碍，需要提高充盈压力以改善心功能者，适宜选用胶体液，以保持血管内容量

McKinley BA, Moore LJ, Sucher JF Computer protocol facilitates evidence-based care of **sepsis** in the surgical intensive care unit. J Trauma 2011 May;70(5):1153-66; discussion 1166-7.

Kaplan-Meier Estimates of the Probability of Survival



The SAFE Study Investigators, N Engl J Med 2004;350:2247-2256

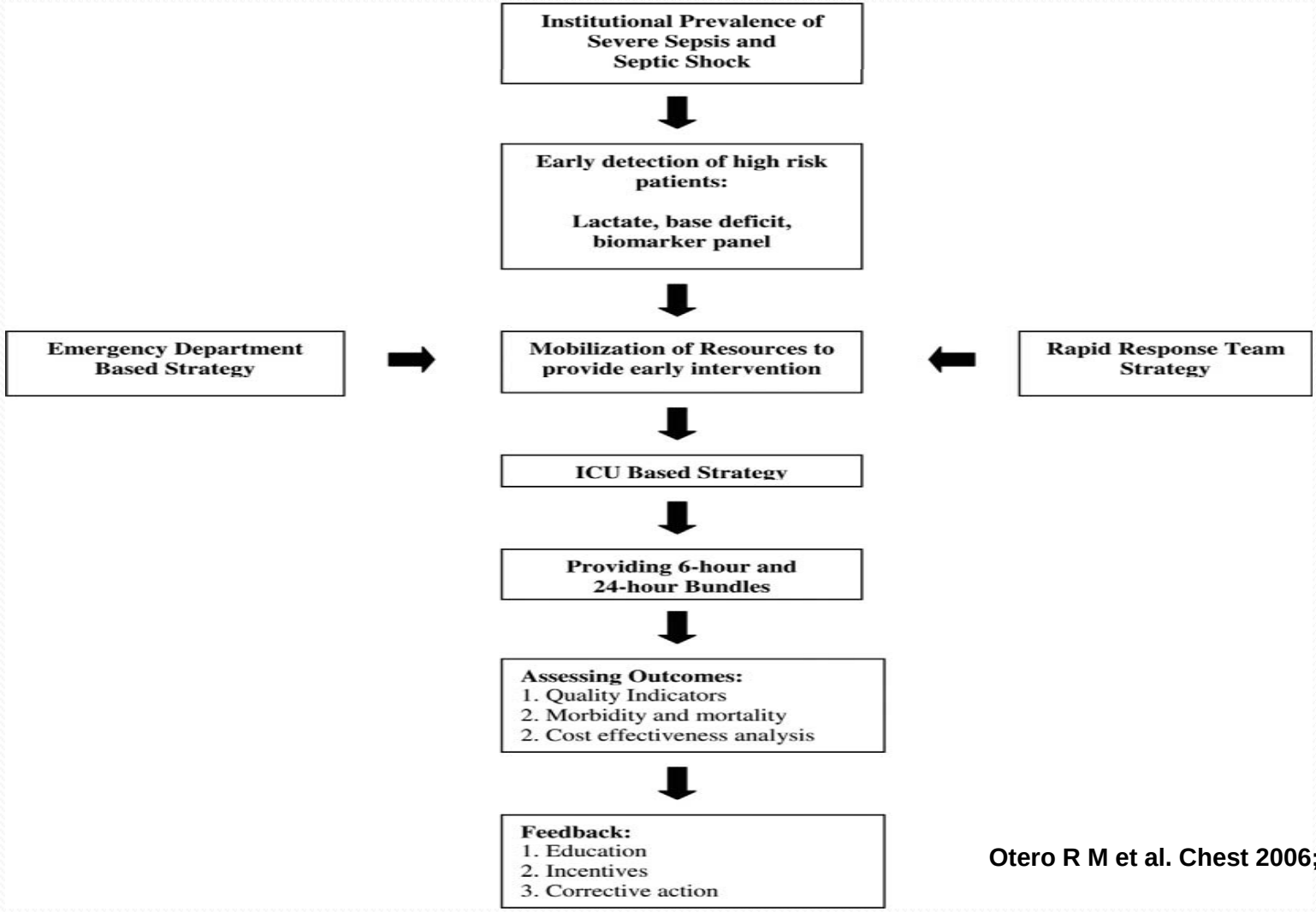
早期抗生素的应用

- Kumar (2006)- retrospectively reviewed over 2000 patients
- Article suggests antibiotics within the first hour of hypotension can affect mortality
- Aggressive, broad antibiotics early is the important thing
- Most rapid antibiotic first
- Kumar (2009)- 5000 patient study
- 20 % patients received inappropriate antibiotics
- Increased mortality by factor of 5

Kumar A, et al, Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock Critical Care Medicine, Volume 34, Issue 6 (June 2006)

Kumar A, et al, Initiation of inappropriate antimicrobial therapy results in a fivefold reduction of survival in human septic shock. Chest 2009 Nov;136(5):1237-48.

An implementation model of EGDT.



Otero R M et al. Chest 2006;130:1579-1595

Early Goal-Directed Therapy in Severe Sepsis and Septic Shock Revisited

- Outcomes Survey: 12 programs
- 1,298 patients with severe sepsis and septic shock
- Treated with EGDT and/or the sepsis bundles
- Pre implementation mortality: 44.8 ± 7.8%
- Post implementation mortality: 24.5 ± 5.5 %

20.3% Reduction in Mortality, NNT 5

Otero RM. et al Chest; 2006:130:1579-1595

EGDT面临挑战

- The major elements of EGDT to achieve a CVP of 8 to 12 cm, followed by the transfusion of packed red cells or an inotropic agent to maintain SvO2 higher than 70%.
- The concept of early resuscitation is a scientifically sound concept, we believe that the major elements of the sepsis bundle are fatally flawed.

Marik PE, Varon J.Early goal-directed therapy: on terminal life support?Am J Emerg Med. 2010 Feb;28(2):243-5.

The Surviving Sepsis Campaign-Highlight

- Resuscitation bundle compliance increased from 10.9 % to 31.3% over 2 years (p <.0001)
- Management bundle compliance improved from 18.4 % to 36.1 % (p = .008)
- Represented mortality decrease from 37 % to 30.8 % (p =.001)

Levy, Mitchell M.; Dellinger, R Phillip; Townsend, Sean R.; et al, The Surviving Sepsis Campaign: Results of an international guideline based performance improvement program targeting severe sepsis, Critical Care Medicine. 38(2):367-374, February 2010.

The Surviving Sepsis Campaign-Highlight

- Directed performance improvement initiative changes practice
- Compliance did improve mortality
- Individual components and mortality benefit need exploration
- Degree of compliance and effect on mortality
- Shows the challenge of compliance
- Explore where to focus efforts

Levy, Mitchell M.; Dellinger, R Phillip; Townsend, Sean R.; et al, The Surviving Sepsis Campaign: Results of an international guideline based performance improvement program targeting severe sepsis, Critical Care Medicine. 38(2):367-374, February 2010.

Traumtic sepsis on the way

- Protocol will change with literature
- Early goal directed therapy still valid/ Likely to change
- Early aggressive antibiotics remain key/ Resistance emerging
- Glycemic control still has benefit
- Drotrecogin alfa remains a select weapon
- Consider adrenal insufficiency in fluid resuscitated shock
- Low tidal volume remains the best practice
- Exciting new therapies/ monitoring on horizon

Dellinger RP, Levy M, et al, Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008 Critical Care Medicine - Volume 36, Issue 1 (January 2008)

谢谢！