

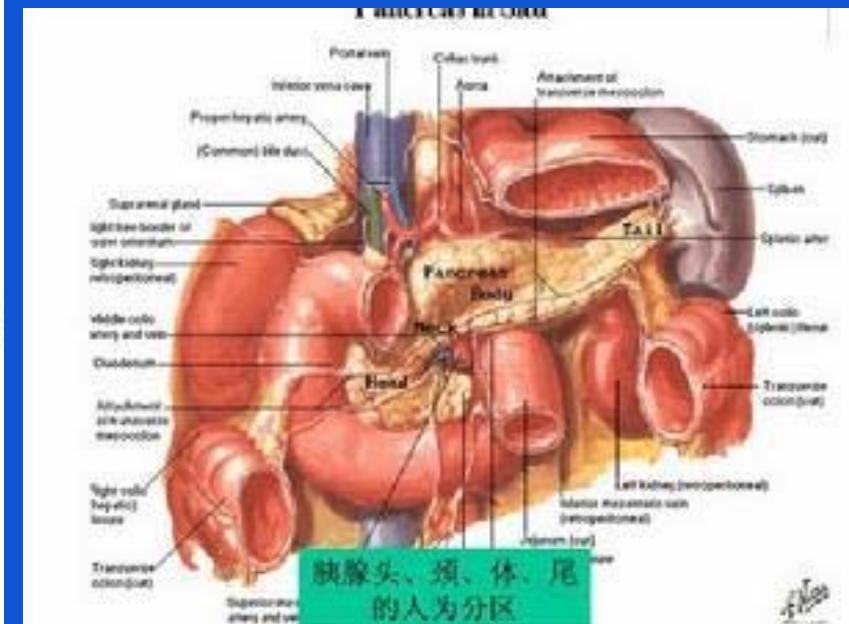
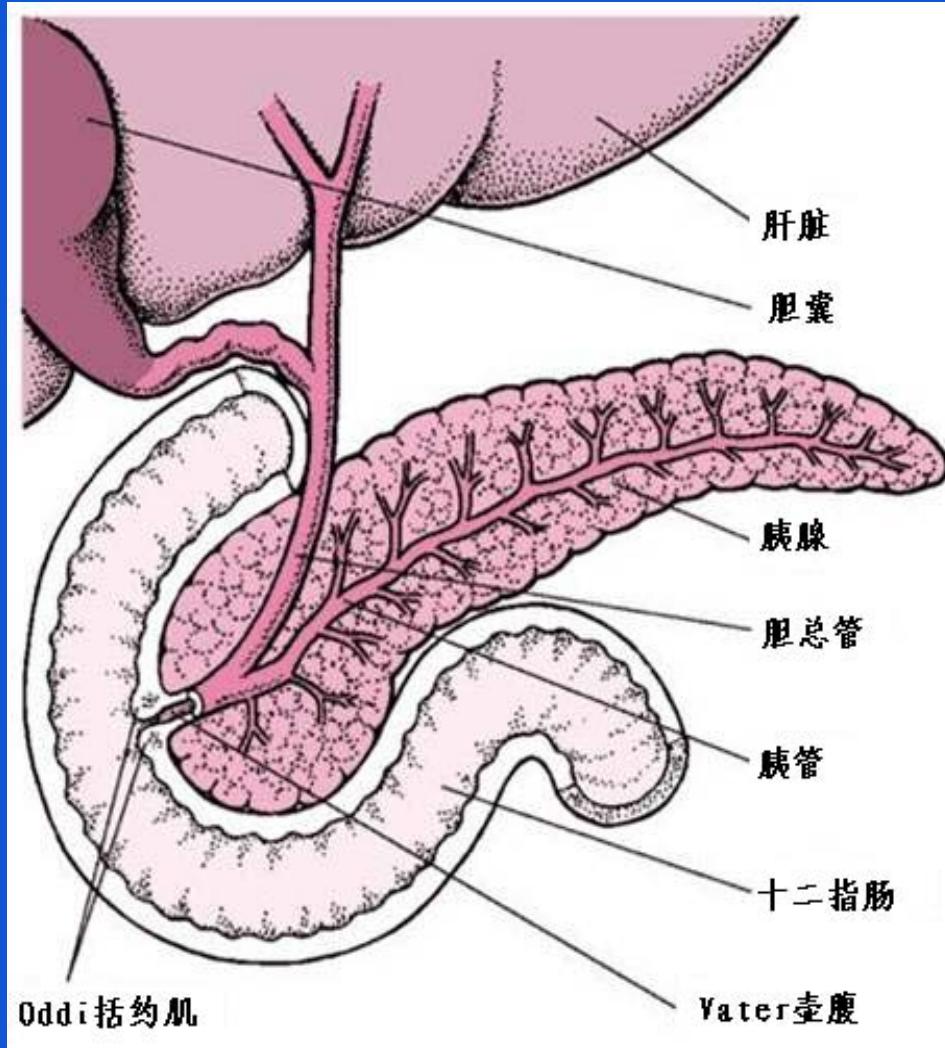
重症急性胰腺炎

早期诊断与治疗原则

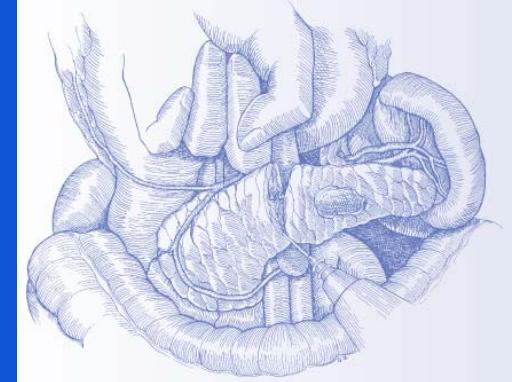
宣武医院普外ICU

陈 宏

胰腺解剖



胰腺功能



外分泌：

- 胰蛋白酶——消化蛋白质
- 胰脂肪酶——消化脂肪
- 胰淀粉酶——消化分解淀粉为葡萄糖

内分泌：

- 胰岛素、胰高糖素——调节血糖
- 胃泌素——活化胃蛋白酶原——消化蛋白质

急性胰腺炎临床诊断标准

(中华医学会外科学会胰腺学组)

- ❖ 定义：急性胰腺炎是胰腺的急性炎症过程，在不同病理阶段，可不同程度地波及邻近组织和其它脏器系统。
- ❖ 临床表现：通常呈急性起病，表现为上腹疼痛，伴有不同程度的腹膜炎体征。常有呕吐、腹胀、发热、心率加快、血白细胞计数上升、血或尿淀粉酶升高。
- ❖ 病理特点：病变程度不等，从显微镜下所见的间质水肿和脂肪坏死，到肉眼可见的胰腺实质或胰周坏死和出血。

急性胰腺炎

急性胰腺炎是胰腺的急性炎症反应，并涉及到局部组织甚至远隔器官。其程度变异很大，从轻微的胰腺实质水肿到出血、坏死、感染、脓肿。因此急性胰腺炎的临床表现也有很大不同：从轻微的腹部不适到出现剧烈腹痛并液体分布异常、低血压、代谢紊乱、全身感染、MODS甚至死亡。

急性胰腺炎

90%急性胰腺炎

- ❖ 轻至中等程度
- ❖ 病程具自限性
- ❖ 支持治疗能完全康复

10%急性胰腺炎

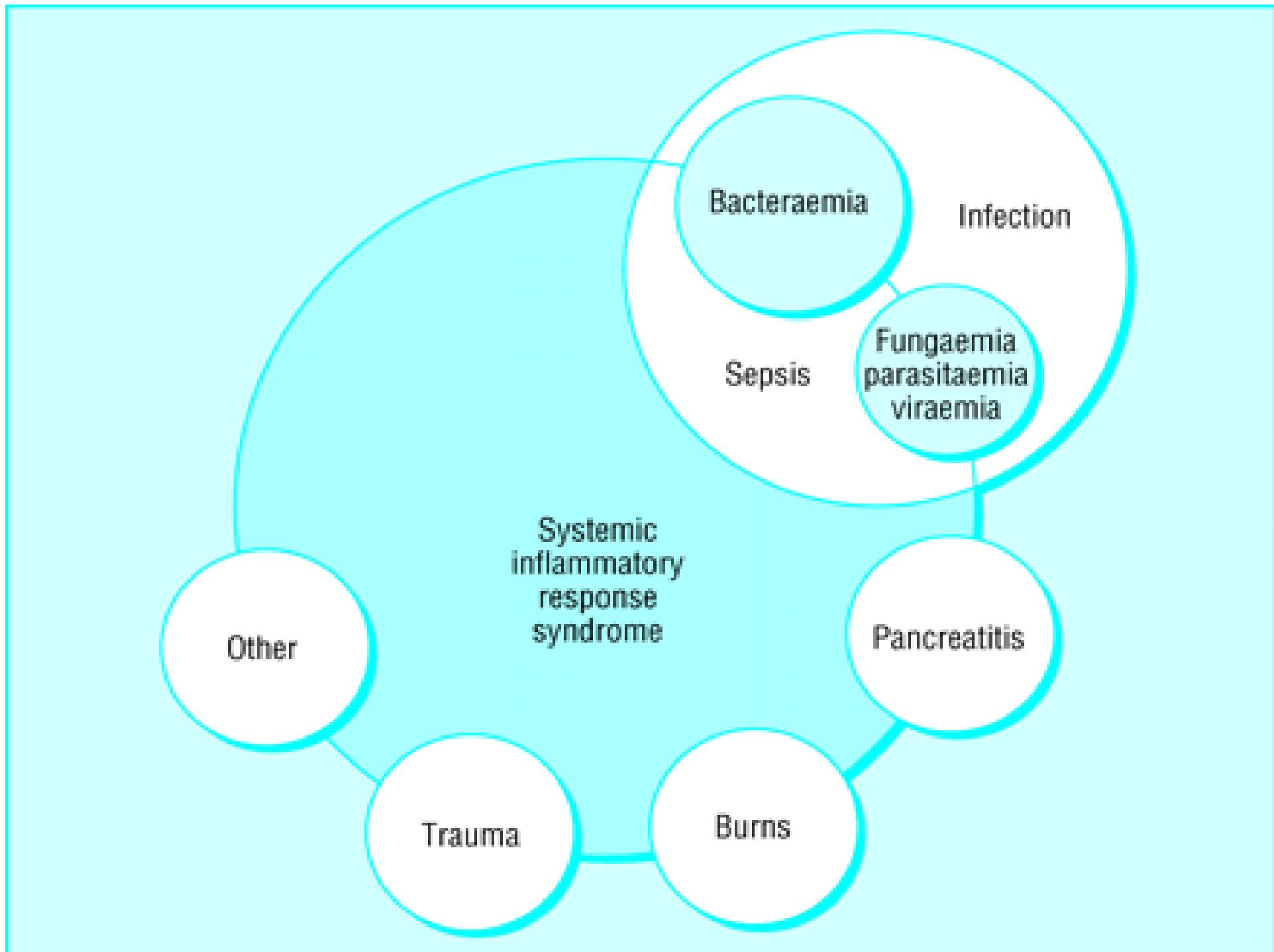
- ❖ 症状严重
- ❖ 较高病死率
- ❖ MODS、感染是主要死亡原因

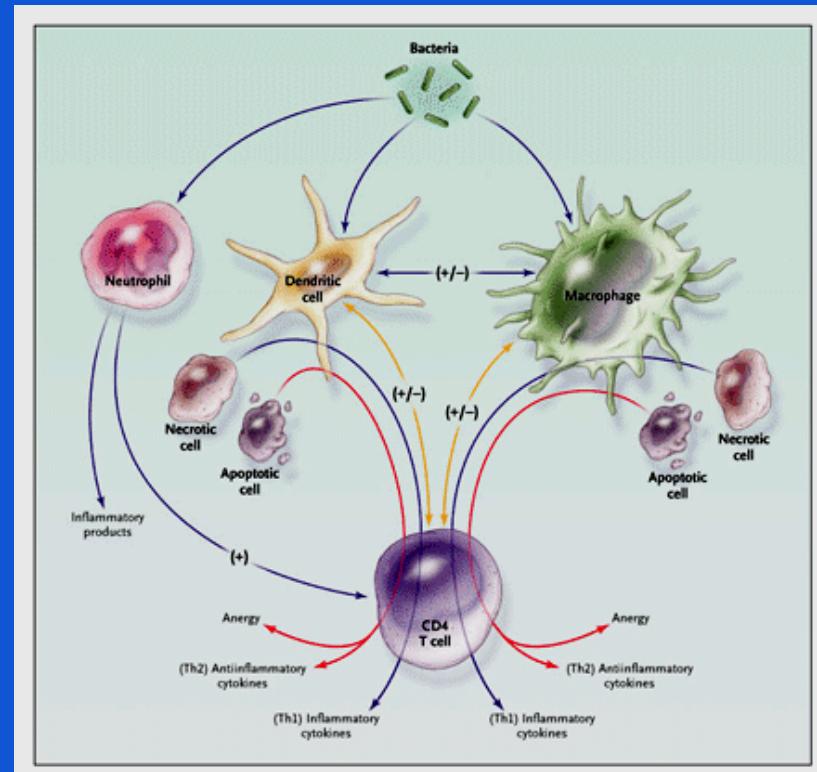
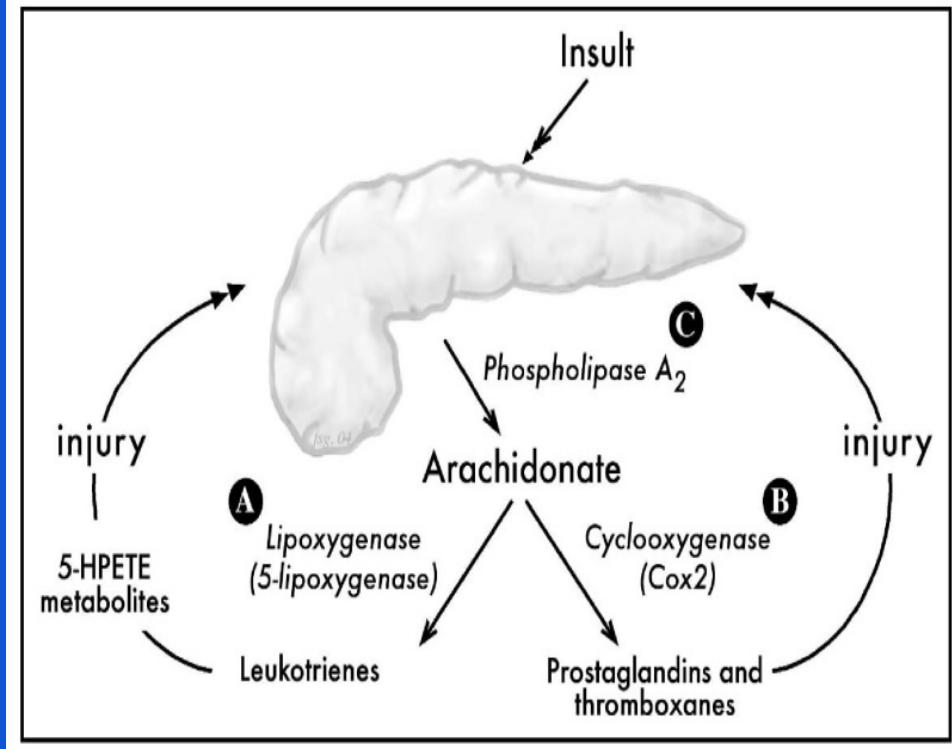
重症急性胰腺炎

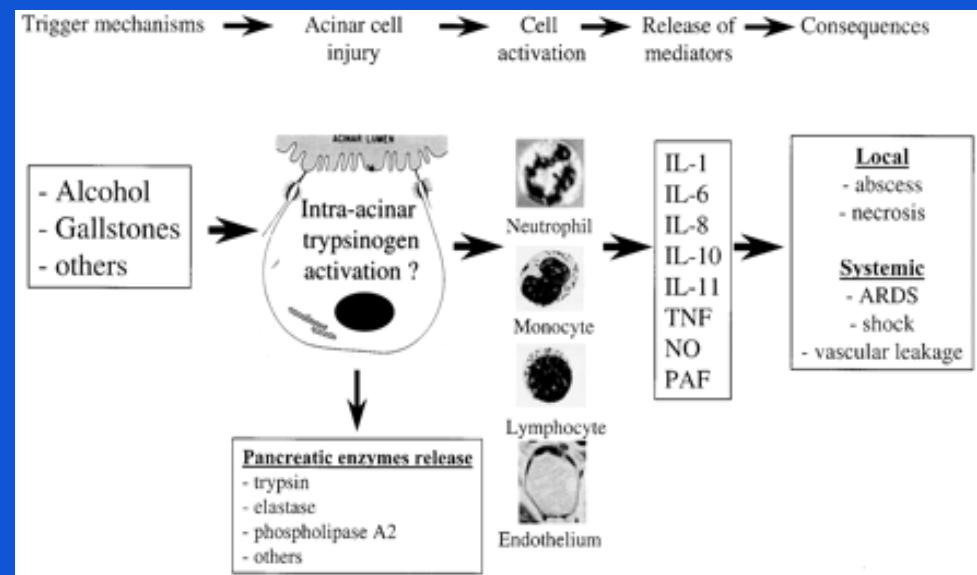
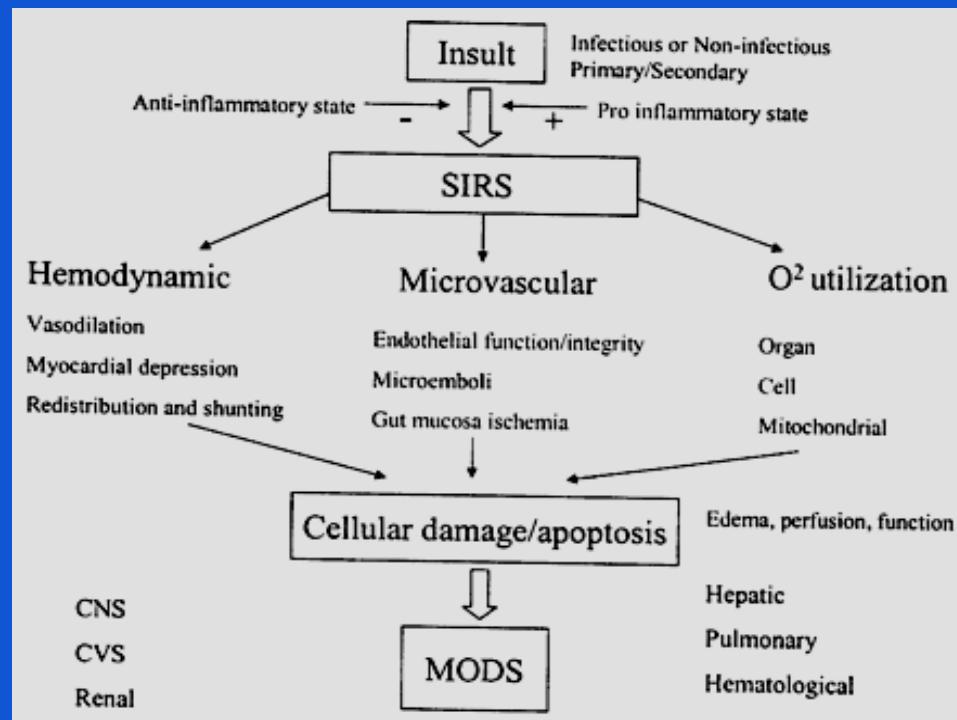
定义：指急性胰腺炎伴有器官功能障碍，或出现胰腺坏死感染、胰周积液（急性液体积聚或假性囊肿）继发感染等局部并发症，或两者兼有。

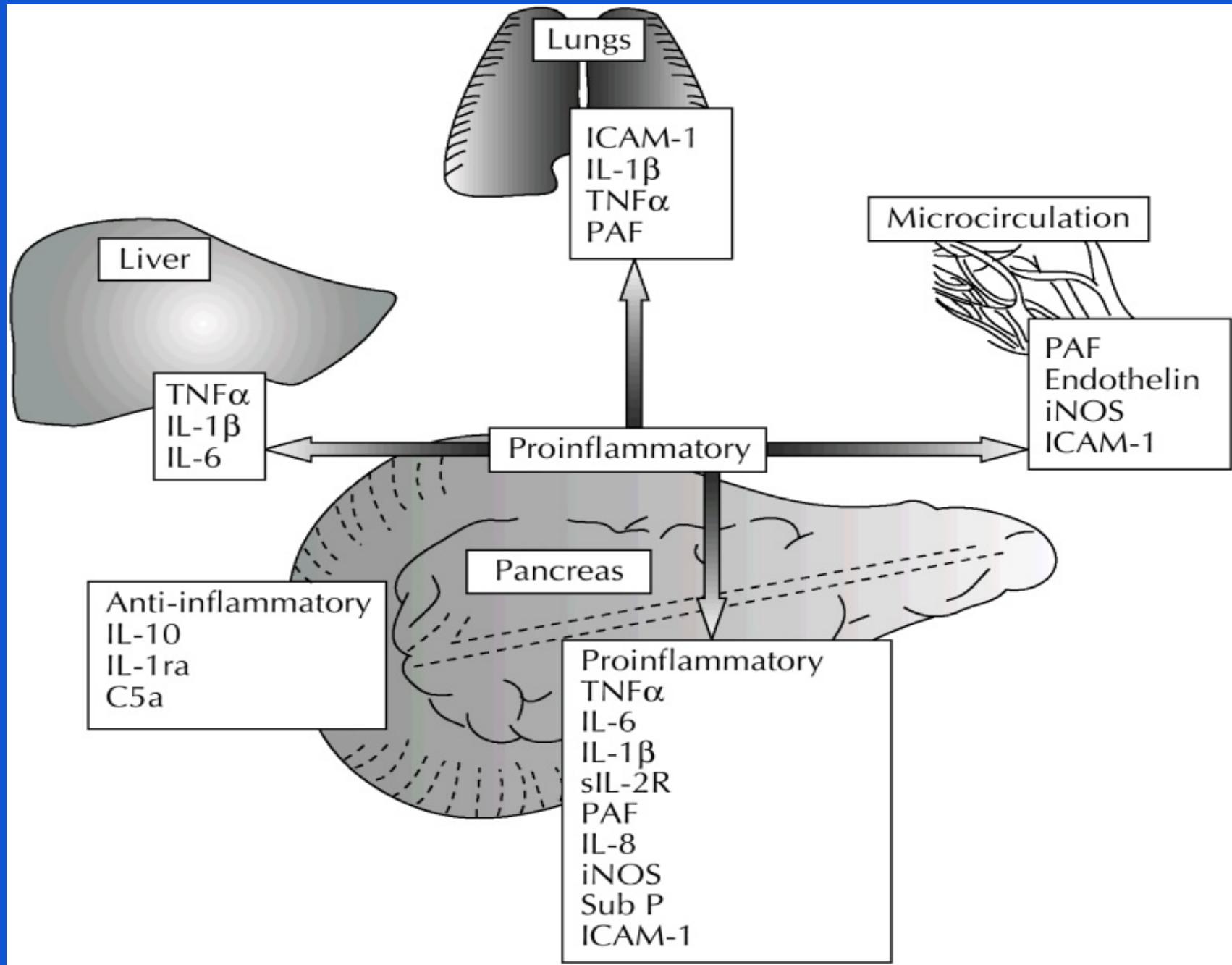
重症急性胰腺炎

- ❖ 临床表现：腹部明显压痛、反跳痛、肌紧张、腹胀、肠鸣音减弱或消失。可有腹部包块，偶见胁腹部瘀斑（Grey-turner）或脐周瘀斑征（Cullen）。
- ❖ 可并发一个或多个器官功能障碍，也可伴严重代谢紊乱，如低钙血症（血钙 7.5mg/dl ）；局部并发症有坏死、感染。APACHE II 评分 ≥ 8 分，Balthazar CT分级系统在Ⅲ或Ⅳ级以上。









病 因

胆道疾病、高脂血症、酒精、高钙血症

遗传因素、创伤（外源、手术、ERCP）

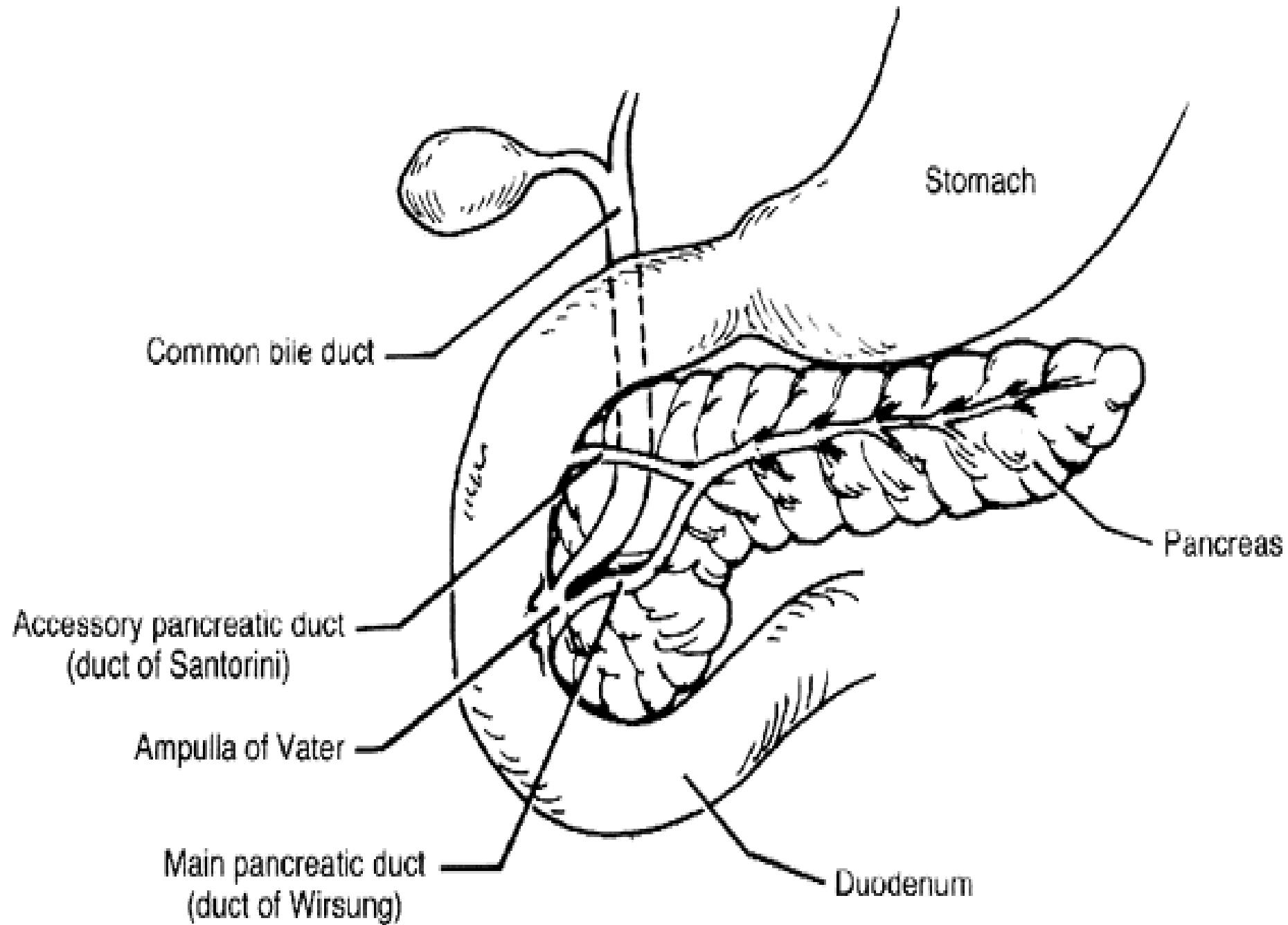
缺血（低血压、体外循环、血管炎、栓塞）、药物

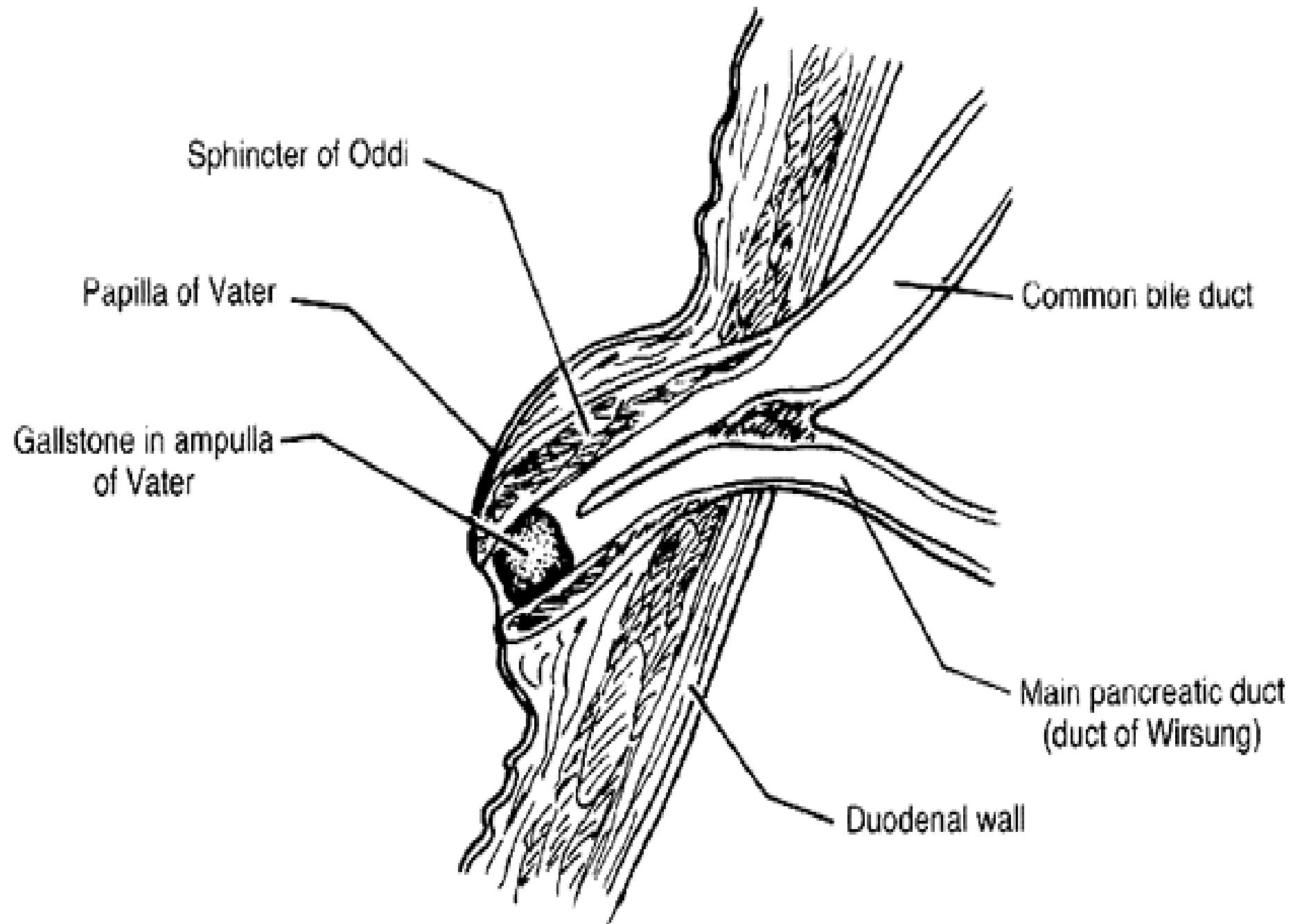
胰管梗阻（肿瘤、囊肿、十二指肠息肉、壶腹狭窄）

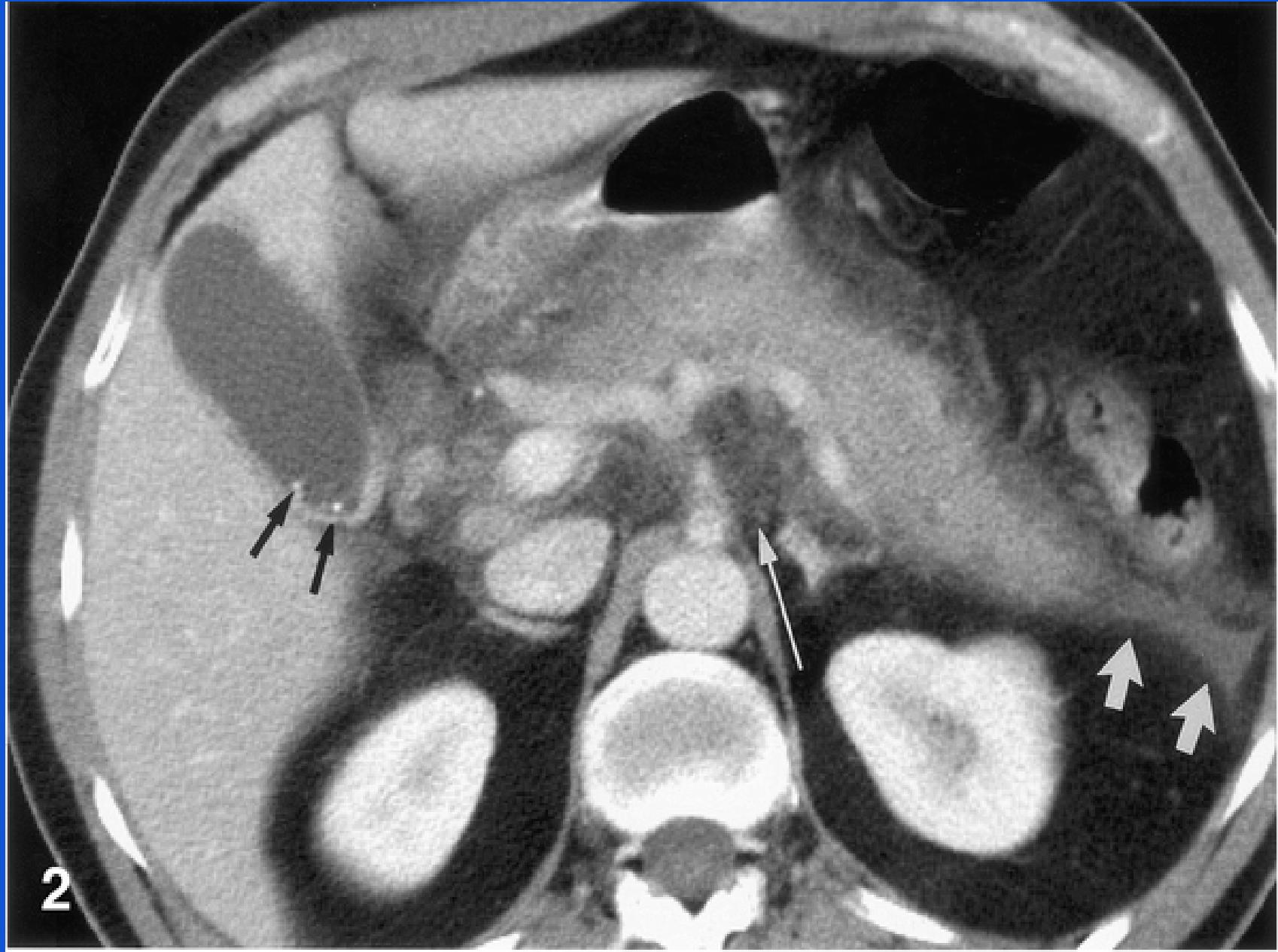
十二指肠梗阻、感染（病毒、霉菌、细菌）、特发

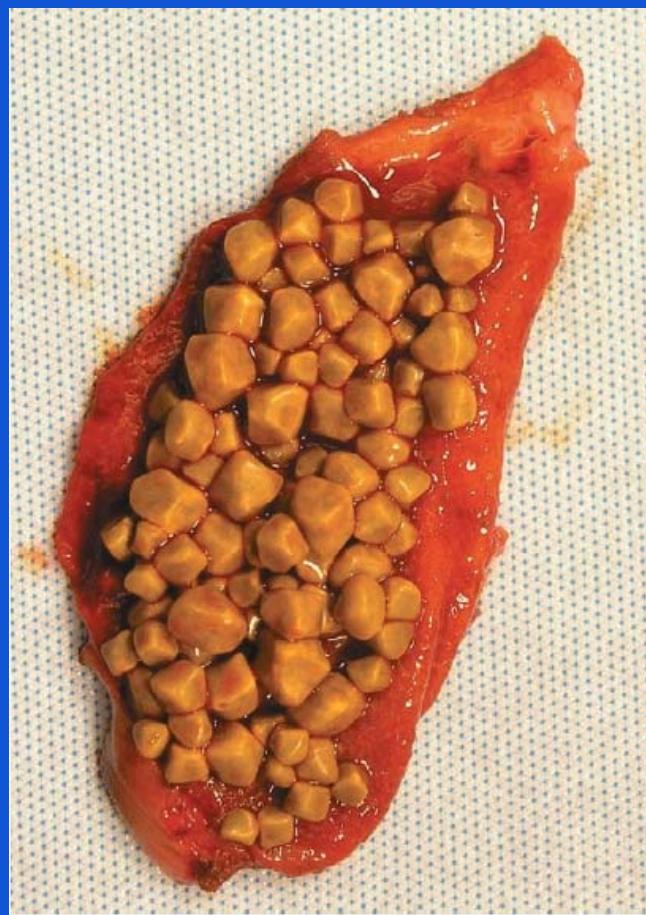
机制

- ❖ 胆源性：胆道梗阻—胰管压高—胰腺细胞损伤
- ❖ 高脂性：胰腺细胞损伤
 - 通透性增加，腺细胞被胰酶、游离脂肪酸、氧自由基等破坏
- ❖ 酒精性：胰腺损伤+Oddi 氏括约肌收缩—胰管高压









实验室诊断

血清淀粉酶

血清淀粉酶同功酶

尿淀粉酶

淀粉酶-肌酐清除率

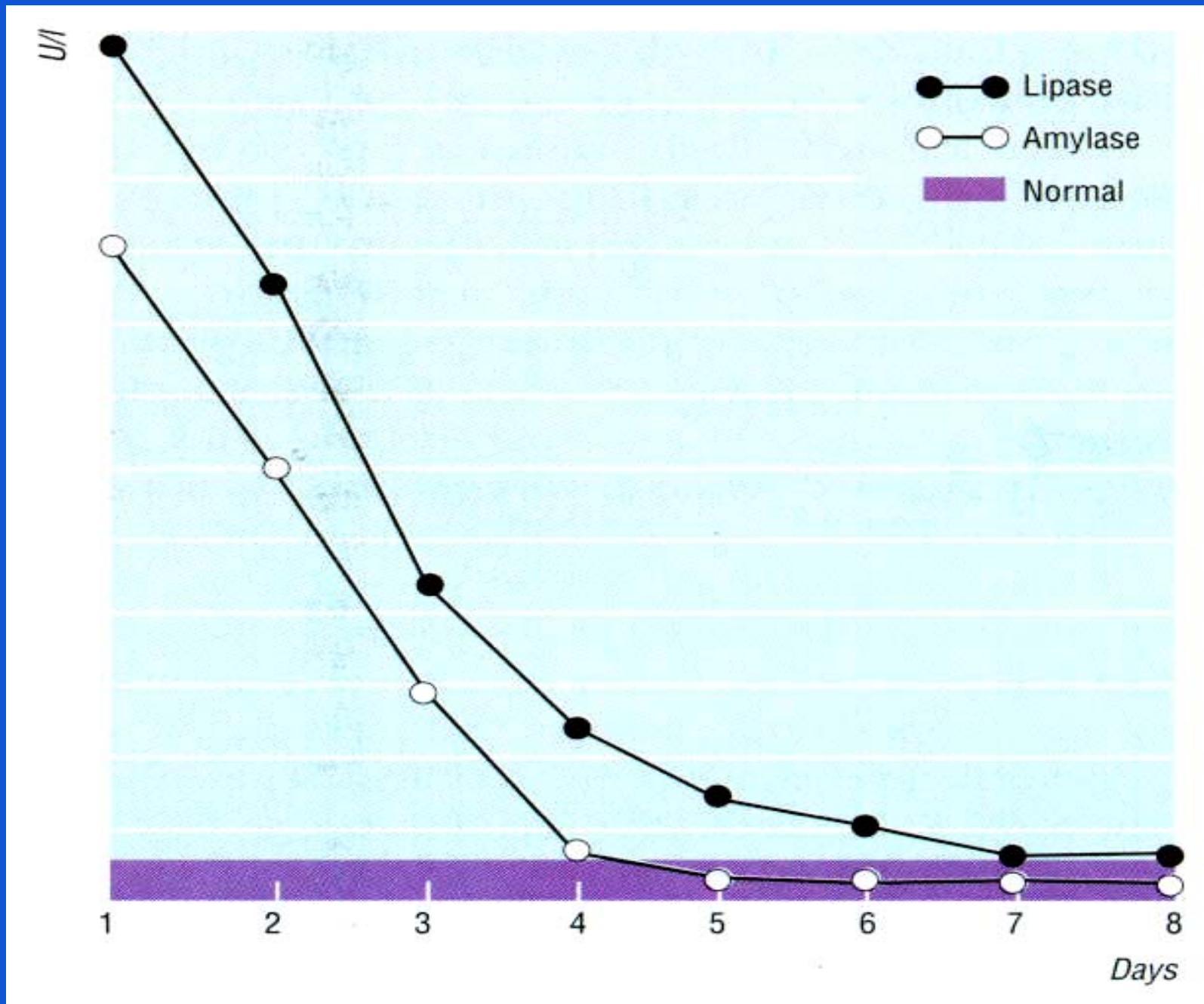
血清脂肪酶

腹穿液检查

乳糜状血

实验室诊断

- ❖ 症状出现24小时内血淀粉酶增高，一周后恢复正常。尿淀粉酶比血淀粉酶持续时间长。淀粉酶升高程度与疾病严重度无关。可有假阳或假阴性结果。其他疾病如消化道穿孔、小肠坏死、急性胆管炎等血淀粉酶也升高。
- ❖ 血脂肪酶比淀粉酶更准确诊断胰腺炎，且升高持续时间长，脂肪酶只有胰腺产生。



放射学检查

胸部X-线平片

腹部X-线平片

超声波检查

CT检查

MRI检查

放射学检查

- ❖ 超声波诊断令人失望，肠内的气体和液体使胰腺显示困难。条件好时可显示胰腺水肿和周围积液
- ❖ 胆石性胰腺炎时超声可检查胆囊或胆管有无结石并测量胆管直径。准确率约70–80%，而CT准确率<50%

放射学检查

CT是诊断急性胰腺炎金标准。口服及静脉用造影剂对比强化使其准确性明显提高。CT分级与临床表现及其严重度相关。CT可显示胰腺坏死、脓肿、胰假性囊肿和胰周积液。

急性胰腺炎CT检查

胰腺改变:	非特异性表现:
胰腺肿胀（局部或弥漫）	肠管扩张
胰腺实质水肿或胰坏死	胸腔渗液
胰周改变:	肠系膜水肿
胰周脂肪模糊	
胰周炎症反应，筋膜增厚	
液体积聚	

胰腺炎非手术治疗

支持治疗	抑制外分泌	抗炎症反应
液体复苏	胃肠减压	自由基清除剂
补充电解质	H ₂ 受体阻滞剂	高流量血滤
镇痛	抗酸剂	抗炎抗体
营养支持	生长抑素	介质受体阻滞剂
促进肠蠕动	新鲜冰冻血浆	PLA ₂ 抑制剂

SAP血流动力学改变

- 低血容量（第三间隙丢失）

- 局部炎症渗出、积液
- 组织水肿、肠腔内

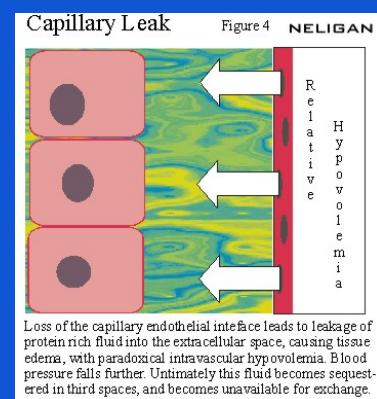
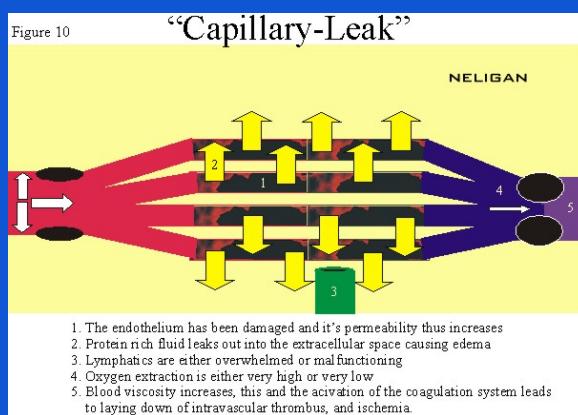
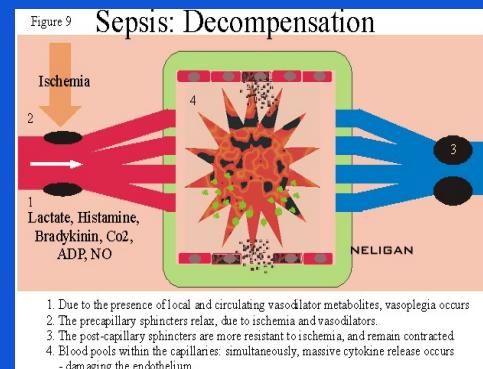
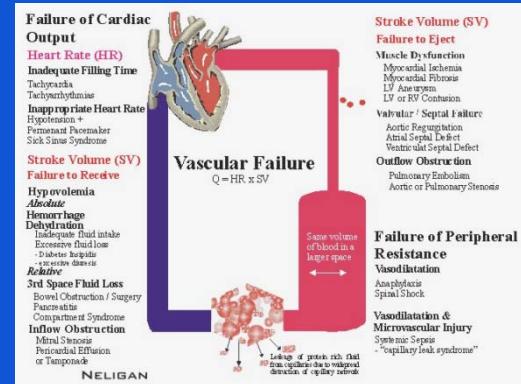
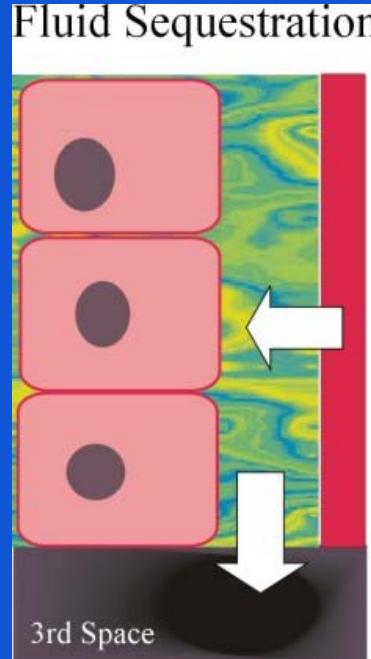
- 血流重新分布（高排低阻）

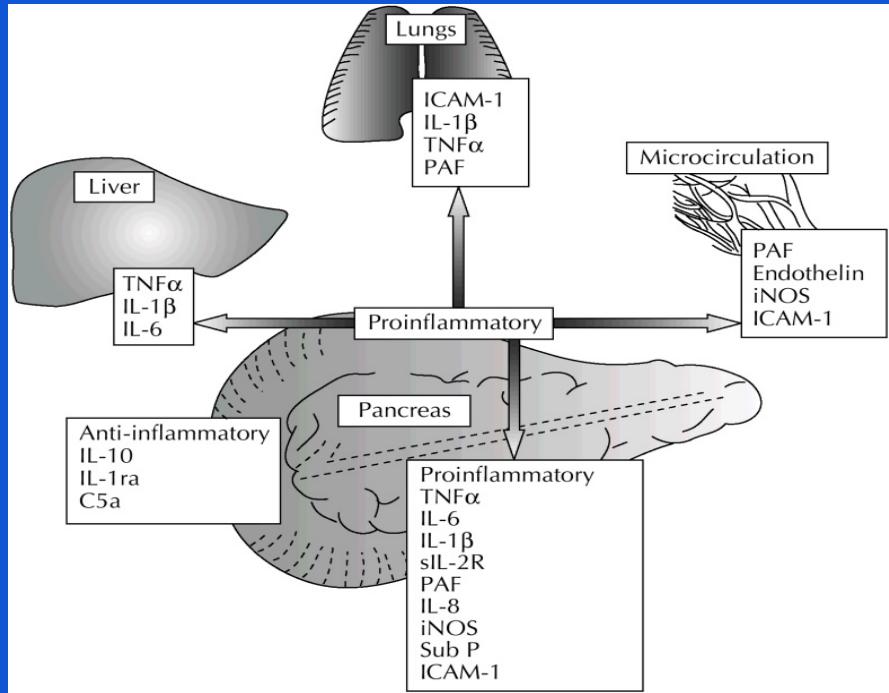
- 血管舒缩
- 心脏舒缩
- 短路、分流
- 凝血/纤溶

- 血管内皮细胞通透性

- 毛细血管渗漏
- 血容量降低

- 心肌细胞收缩、传导抑制

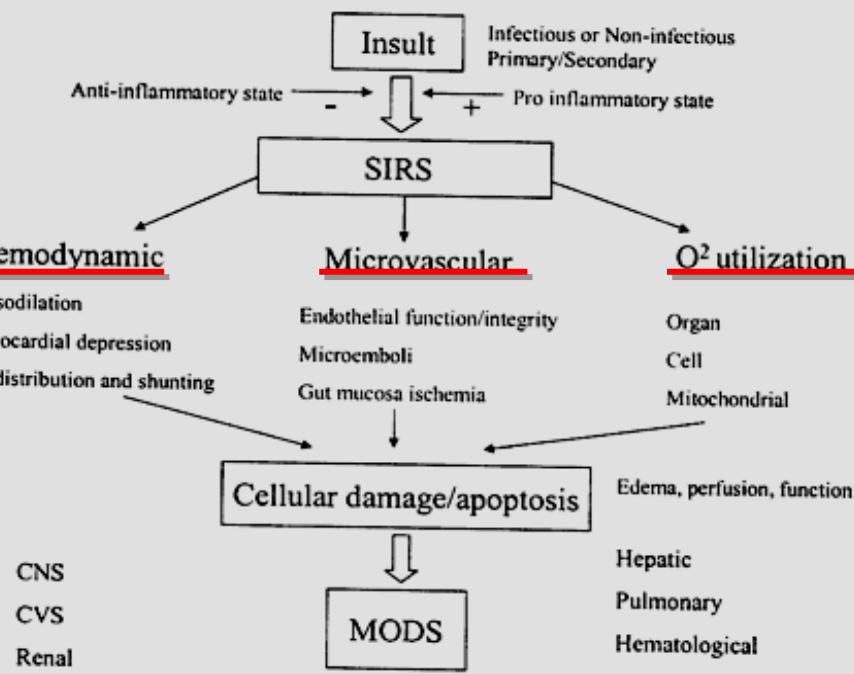




早期液体治疗目的

- ❖ 纠正低血容量状态
- ❖ 改善组织血流灌注和氧合水平
肠粘膜灌注/屏障/抑炎/细菌移位
- ❖ 减轻或避免器官功能损害
- ❖ 降低早期病死率

• 胰腺坏死？胰腺感染？中后期病死率？



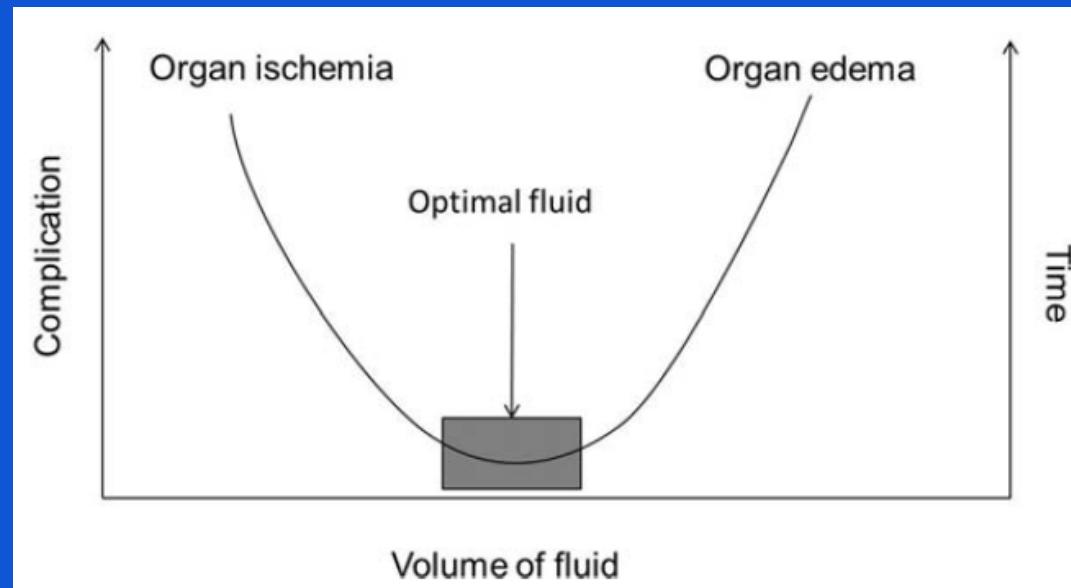
实现目标→达到目的

- ❖ 液体治疗策略——目标制订与实现目标
- ❖ 心率、脉搏、血压、尿量
- ❖ CVP、MAP、PAWP (静态)
- ❖ ITBI、CI、EVLW、GEDV (静态)
- ❖ PPV、SVV、SPV、PLRT (动态)
- ❖ ScvO2、Phi、乳酸、碱剩余

液体治疗

双刃剑

- ❖ 不足: 器官功能损害、死亡
- ❖ 过度: 器官功能损害、死亡



A positive fluid balance is associated with a worse outcome in patients with acute renal failure

Critical Care 2008, 12:R74

Hazard ratios: results of multivariate Cox regression analysis for 60-day mortality in critically ill patients with acute renal failure			
Characteristic	Hazard ratio	95% CI	P value
Age	1.02	1.01–1.03	<0.001
SAPS II (per point)	1.03	1.02–1.04	<0.001
Heart failure	1.38	1.05–1.81	0.02
Medical admission	1.68	1.35–2.08	<0.001
Mean fluid balance, L/24 hours	1.21	1.13–1.28	<0.001
Mechanical ventilation	1.55	1.14–2.11	<0.001
Liver cirrhosis	2.73	1.88–3.95	<0.001

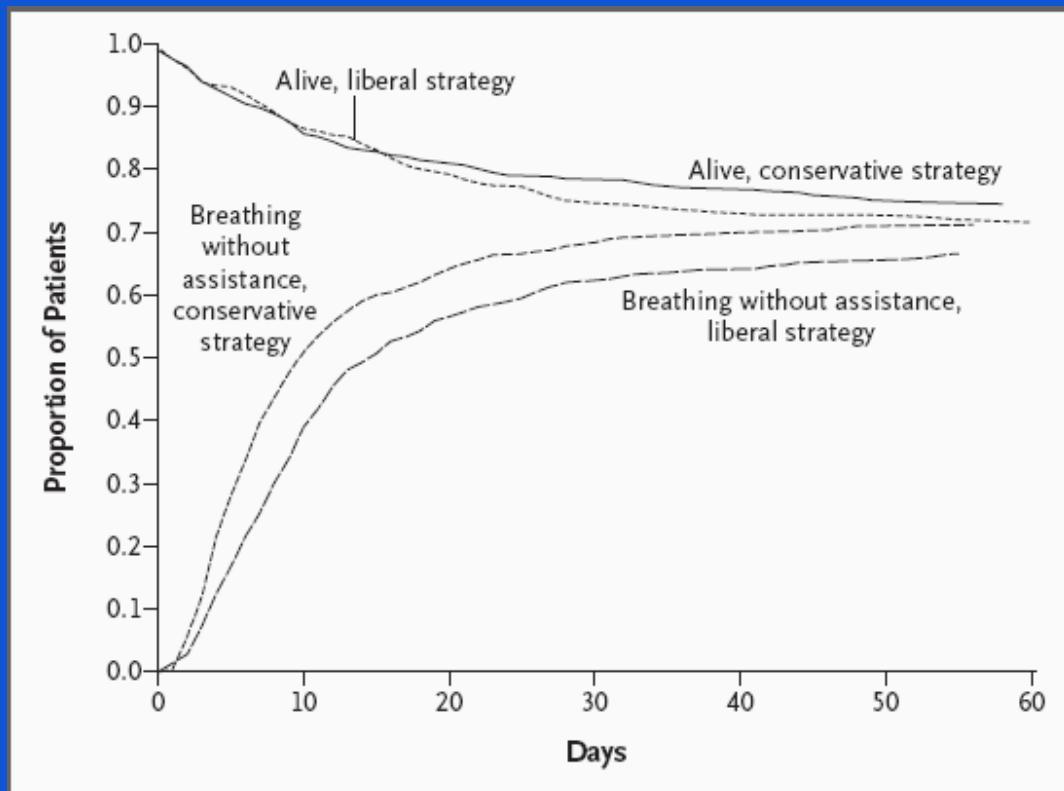
CI, confidence interval; SAPS II, Simplified Acute Physiology Score II.

Mean fluid balance was significantly more positive in patients with early and late ARF than in patients without ARF throughout the first 7 days of the ICU stay.

Mean fluid balance was retained as an independent predictor of mortality.

Comparison of two fluid-management strategies in ALI ARDS Network Clinical Trials

N Engl J Med. 2006; 354(24):2564-2575



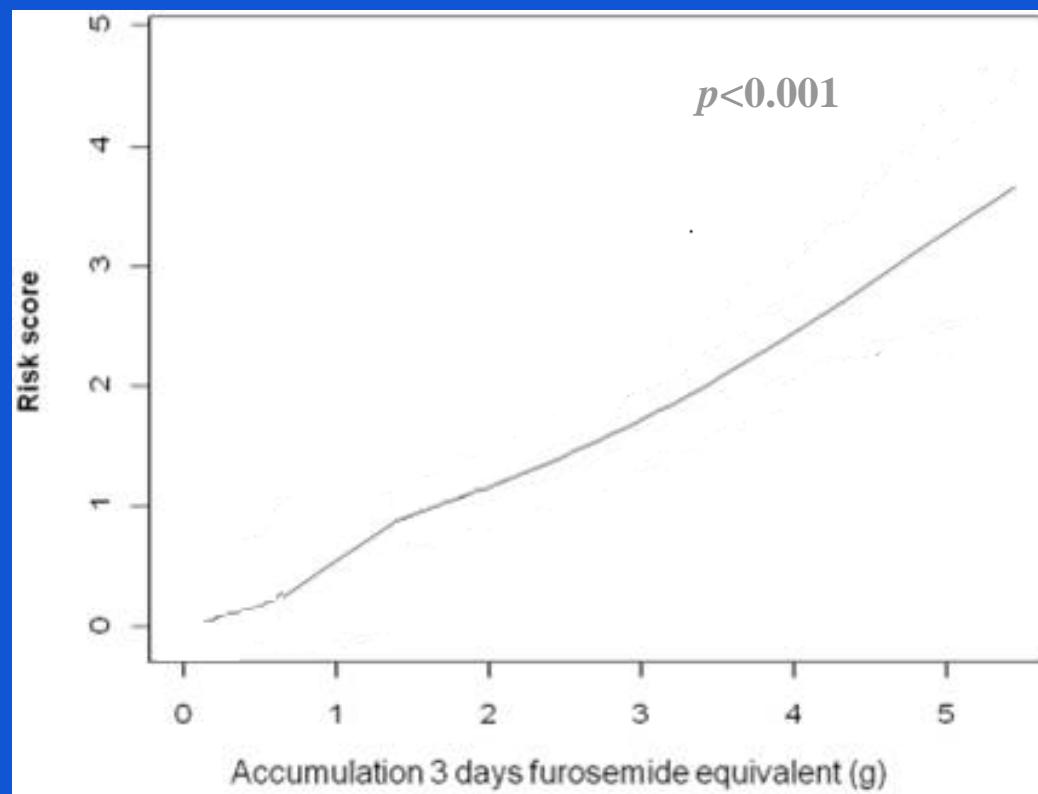
A randomized study of comparing conservative and liberal fluid management for **1000** ALI patients.

The conservative strategy of fluid management improved lung function, but did not increase the use of dialysis.

Effect of diuretic use on 30-day postdialysis mortality in critically ill patients receiving acute dialysis

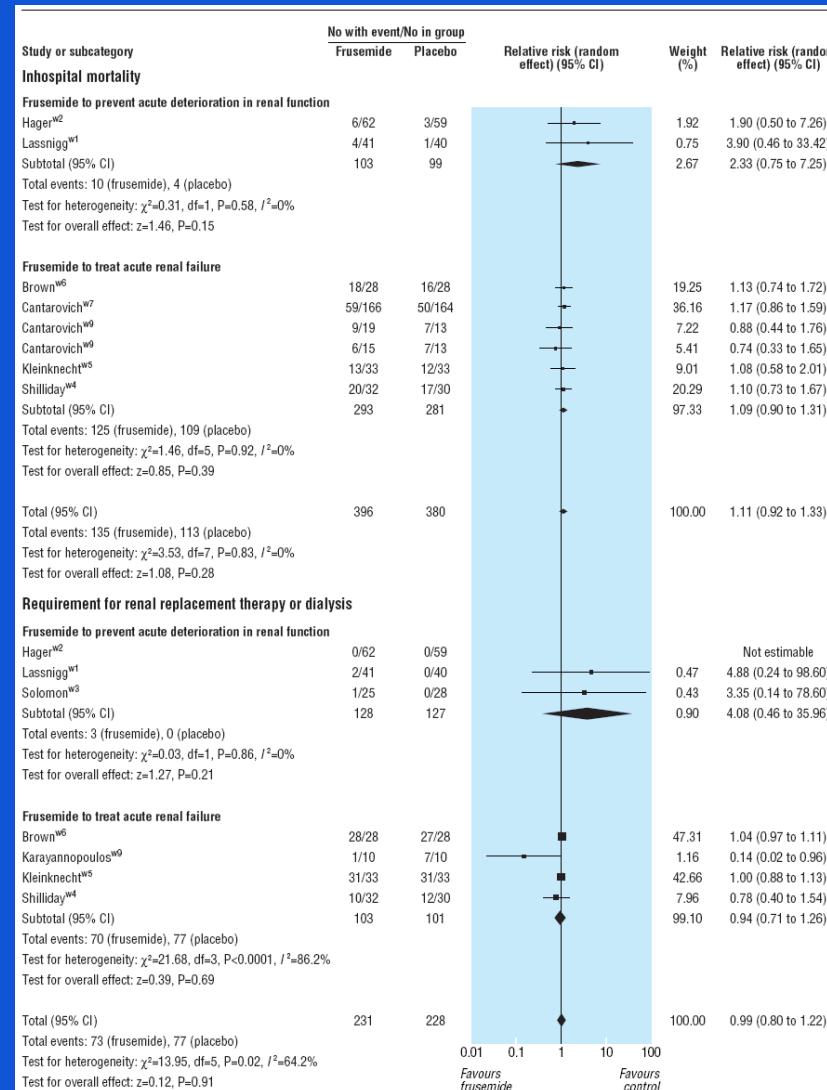
prospective, multicenter, observational study, 572 patients with postsurgical acute kidney injury receiving hemodialysis

Accumulated diuretics dose predicts post dialysis 30 days mortality



Meta-analysis of frusemide to prevent or treat acute renal failure

9 RCTs totalling 849 patients with or at risk of acute renal failure



Frusemide is not associated with any significant clinical benefits in the prevention and treatment of AKI.

Frusemide is not associated with improved mortality or rate of independence from RRT

High doses may be associated with an increased risk of ototoxicity

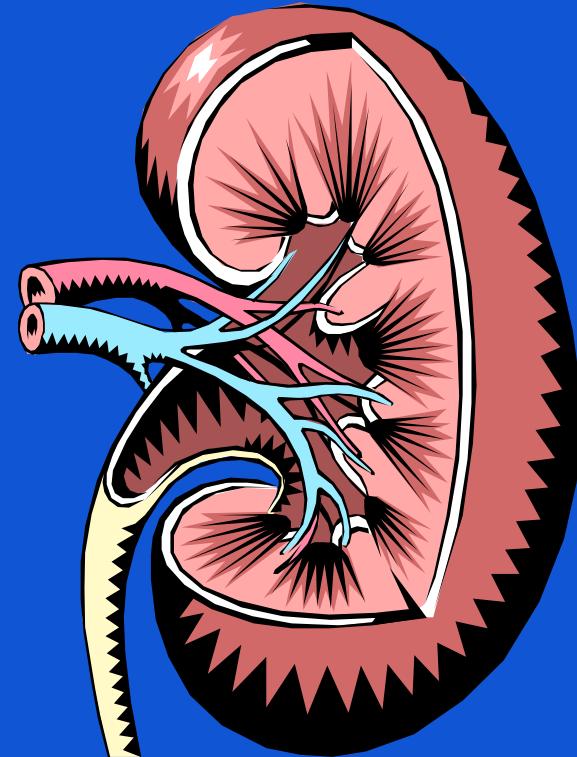
动脉
静脉



静脉

滤出液

- ❖ RRT模拟肾小球工作方式
- ❖ 在几小时,甚至几天的时间,清除机体多余的水、代谢产物, 调节酸碱和电解质的平衡——机体内环境稳定

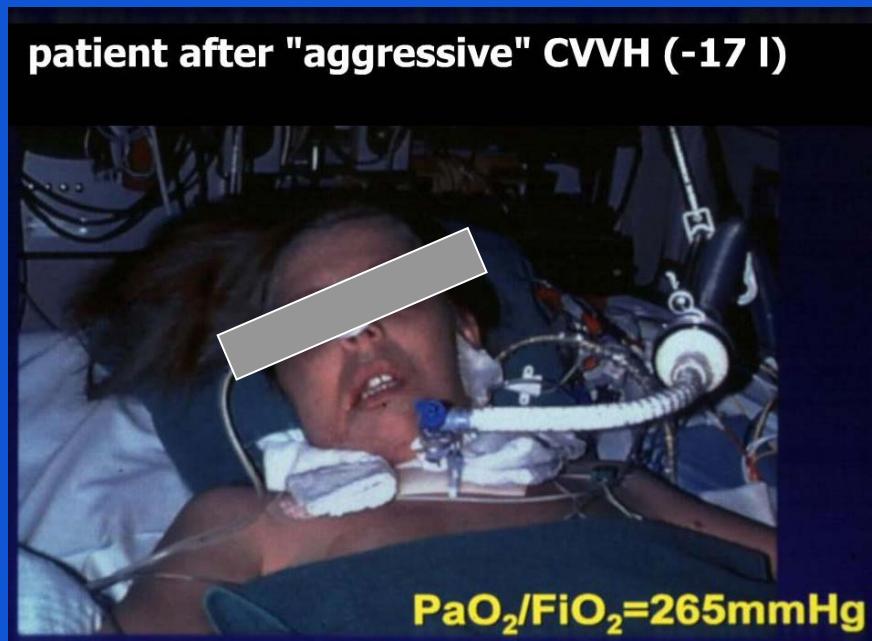


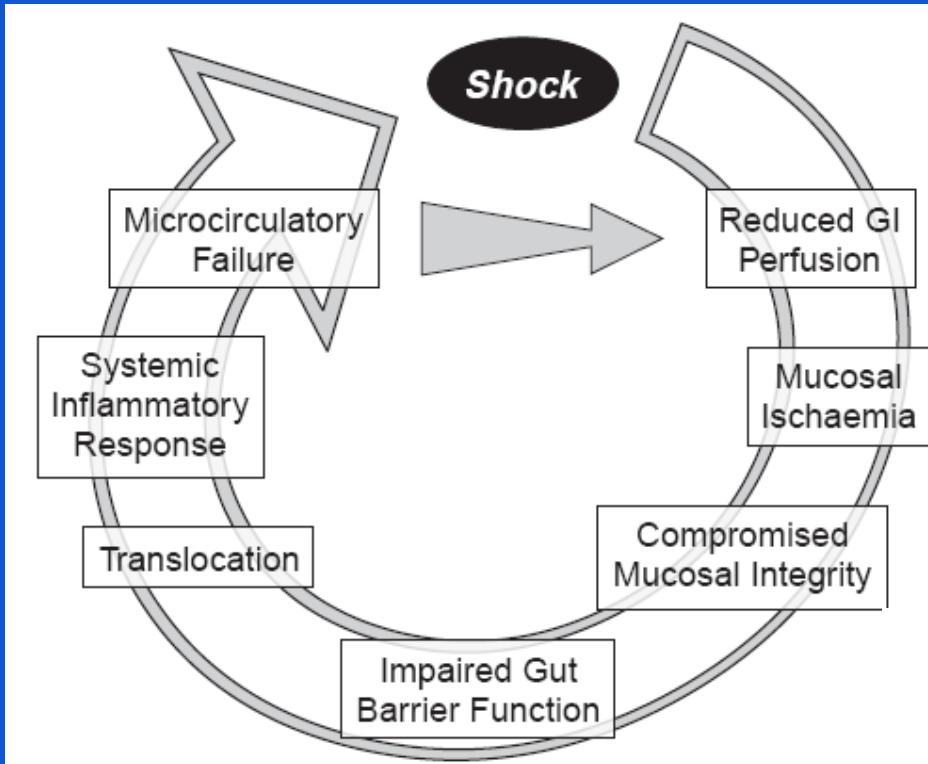
IAH/ACS Management: Consider Hemofiltration

Fluid Overloaded

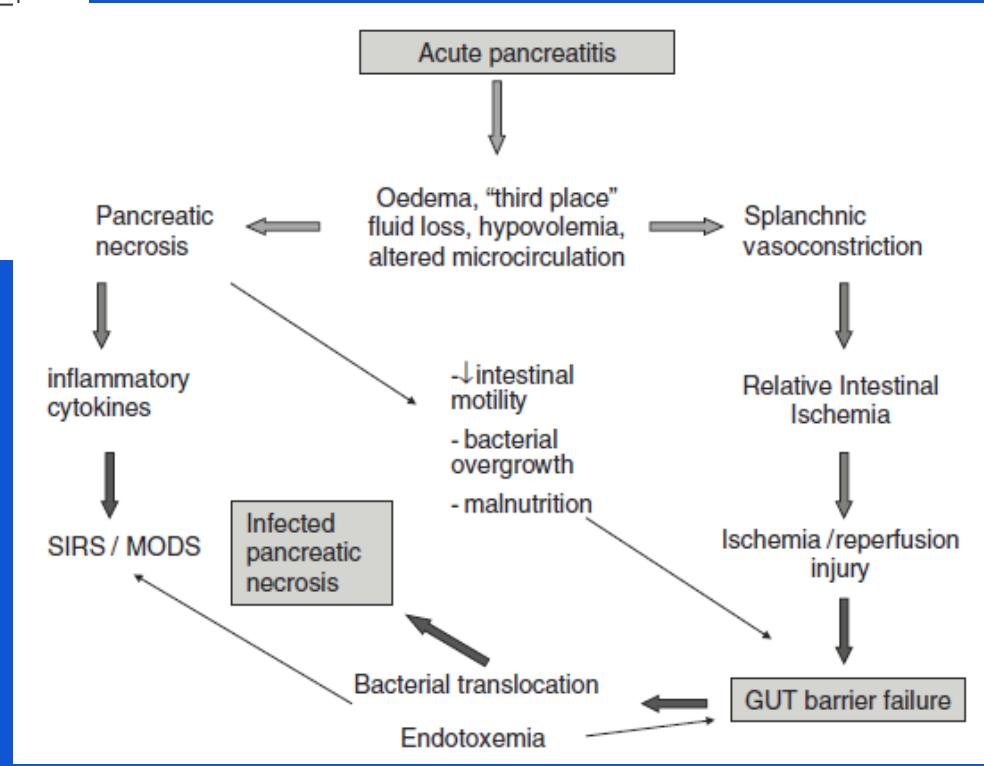


Post CVVH





Cascade of pathophysiological processes triggered by shock.



SAP——胃肠道动力障碍

- ❖ 胃肠运动抑制
胃潴留、肠麻痹
- ❖ 胃肠功能不全
肠黏膜上皮细胞过度凋亡
- ❖ 肠黏膜屏障功能障碍
肠壁通透性增加

胃肠动力学恢复是改善SAP预后关键措施

胃肠功能支持方法

- ❖ 液体治疗：改善肠粘膜灌注/氧合
- ❖ 机械性刺激肠蠕动：硫酸镁、中药、灌肠
- ❖ 促进蠕动药物：新斯的明、吗丁啉等
- ❖ 针灸：针刺足三里等穴位
- ❖ 理疗：超短波
- ❖ 排便**2-4次/日，<1000ml**



Table 3. Comparisons of LPS and L/M ratio between two groups
(mean \pm SD)

Variables	On admission	Day 1	Day 3	Day 5	Day 7
L/M					
Study (<i>n</i> =20)		0.47 \pm 0.17	0.42 \pm 0.18	0.26 \pm 0.18	0.15 \pm 0.20
Control (<i>n</i> =20)		0.50 \pm 0.23	0.48 \pm 0.24	0.40 \pm 0.26	0.34 \pm 0.27
<i>P</i> values		0.665	0.456	0.076	0.001
LPS (EU/ml)					
Study (<i>n</i> =20)	0.61 \pm 0.19	0.49 \pm 0.24	0.33 \pm 0.22	0.19 \pm 0.22	0.12 \pm 0.21
Control (<i>n</i> =20)	0.58 \pm 0.24	0.55 \pm 0.24	0.45 \pm 0.26	0.35 \pm 0.27	0.26 \pm 0.29
<i>P</i> values	0.665	0.473	0.129	0.006	0.008

Table 4. Comparisons of CRP, IL-6 and TNF- α between two groups (mean \pm SD)

Variables	On admission	Day 1	Day 3	Day 5	Day 7
CRP (mg/dl)					
Study (<i>n</i> =20)	11.83 \pm 4.55	15.42 \pm 4.82	13.81 \pm 4.45	9.14 \pm 4.34	6.02 \pm 4.65
Control (<i>n</i> =20)	10.66 \pm 4.24	14.11 \pm 3.80	15.86 \pm 3.60	13.16 \pm 4.31	9.16 \pm 6.29
<i>P</i> values	0.402	0.499	0.053	0.002	0.038
IL-6 (pg/ml)					
Study (<i>n</i> =20)	44.22 \pm 24.52	33.68 \pm 22.04	20.97 \pm 17.47	13.20 \pm 14.55	8.14 \pm 12.68
Control (<i>n</i> =20)	40.58 \pm 30.32	35.24 \pm 30.67	29.00 \pm 28.23	21.98 \pm 25.43	17.39 \pm 22.94
<i>P</i> values	0.358	0.685	0.387	0.194	0.034
TNF-α (pg/ml)					
Study (<i>n</i> =20)	107.52 \pm 51.49	89.74 \pm 57.89	63.20 \pm 55.09	43.43 \pm 54.11	30.86 \pm 54.51
Control (<i>n</i> =20)	88.10 \pm 63.04	77.70 \pm 61.03	67.33 \pm 61.51	64.13 \pm 70.21	55.51 \pm 66.16
<i>P</i> values	0.126	0.365	0.871	0.330	0.086

腹腔压力

- ❖ 腹腔内压（**IAP**）：密闭腹腔内压力
- ❖ 影响**IAP**因素
 - 腹腔内器官容积
 - 占据空间病变
 - ❖ 血液、腹水、肿瘤
 - 腹壁顺应性
- ❖ IAP增高常见于ICU患者



SAP致IAH/ACS原因

- ❖ 胰腺、胰周、腹膜后炎症，水肿
- ❖ 胰周、腹腔、腹膜后液体积聚、脓肿
- ❖ 胃肠道水肿、蠕动减退、麻痹、肠梗阻
- ❖ 腹腔内实质器官水肿
- ❖ 液体治疗中大量液体输注
- ❖ 腹腔内出血、填塞止血、勉强关腹

2014-4-14

chenhong



THE SYSTEMIC EFFECTS OF IAP

CNS

- ↑ ICP
- ↓ CPP

Cardiovascular

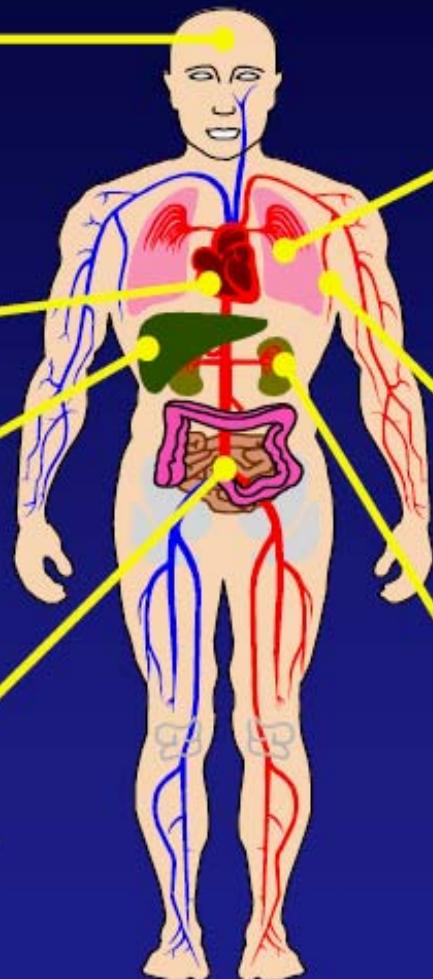
- hypovolemia
- ↓ venous return
- ↓ CO
- ↑ SVR
- ↑ PAOP, CVP

Hepatic

- ↓ portal blood flow
- ↓ lactate clearance

Gastrointestinal

- ↓ celiac / SMA blood flow
- ↓ mucosal blood flow
- ↓ pH



Pulmonary

- ↑ PIP, Paw
- ↑ Qsp/Qt, Vd/Vt
- ↓ compliance
- atelectasis
- hypoxia
- hypercarbia

Thoracoabdominal

- elevated diaphragm
- ↑ intrathoracic pressure
- IVC distortion
- ↓ wall compliance
- ↓ abd wall blood flow

Renal

- ↓ renal blood flow
- ↓ UOP
- ↓ GFR

IAH/ACS治疗原则

- ❖ 监测IAP
- ❖ 维持组织灌注和器官功能
- ❖ 降低IAP措施
 - 改善腹壁顺应性
 - 胃肠减压/减少胃肠内容物
 - 引流腹内积液
 - 适当液体平衡
- ❖ 难于纠正IAH立即手术减压

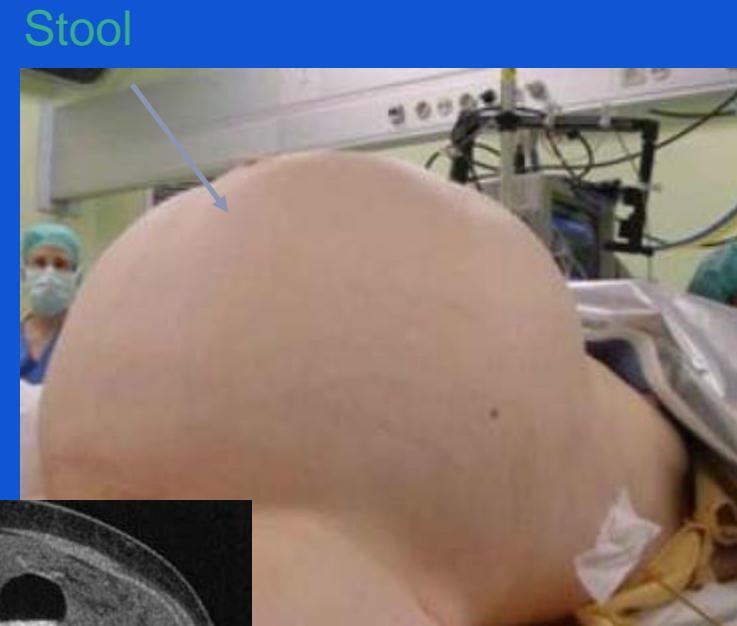
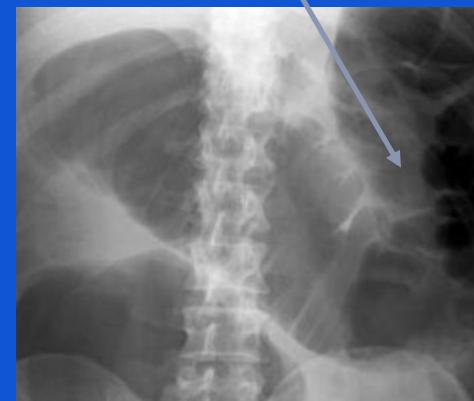


Improve abdominal wall compliance

Ensure Adequate sedation and analgesia
(Step 1)

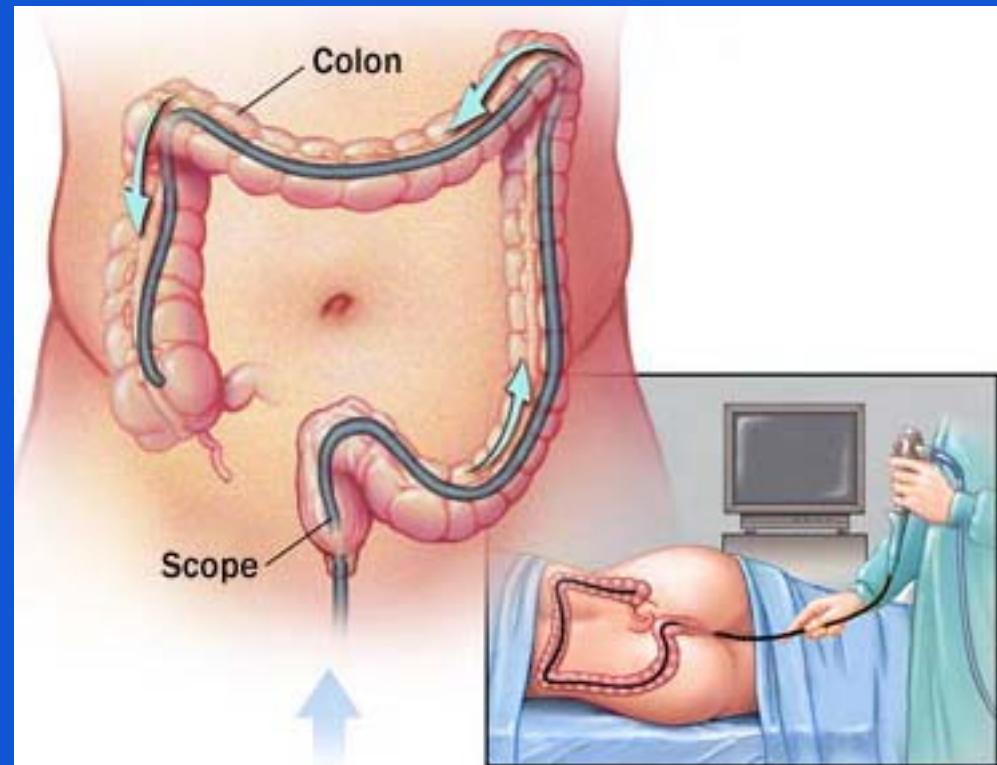


IAH/ACS Management : Evacuate Bowel, Peritoneal Fluids



清除肠内容物

可考虑结肠镜减压

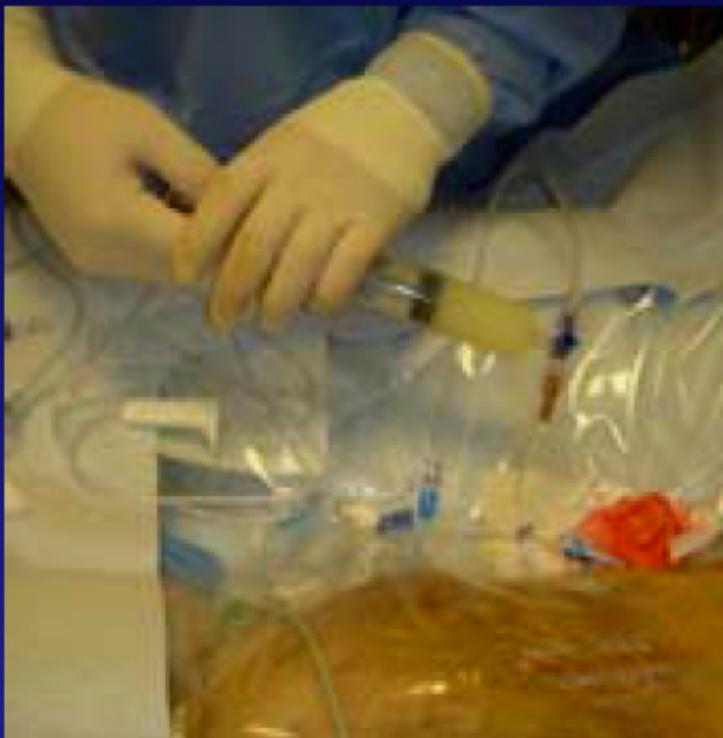


Evacuate Extraluminal space occupying lesions

Use bedside ultrasound to identify lesions/fluid that might be removable (Step 1)



CASE PRESENTATION



- 900 mL milky ascites aspirated using a central venous catheter placed above the liver
- 1 hour post-paracentesis
 - BP 150/80, HR 110
 - SaO₂ 0.93, FiO₂ 0.70
 - UOP: 35 mL/hr
 - ABG: 7.27/70/64/3.9
 - IAP 14 mmHg
 - Decompression was avoided

Evacuate Intraluminal contents

Initiate gastro/colonic prokinetic agents (Step 1)

Erythromycin 200 mg IV q 8 h

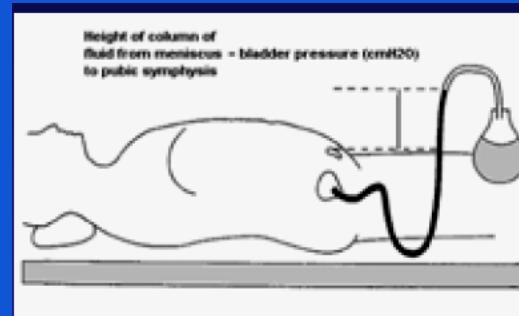
Metoclopramide 10 mg IV q 6 h

Neostigmine 1–2 mg IV slow infusion



胃肠减压/减少胃肠内容物

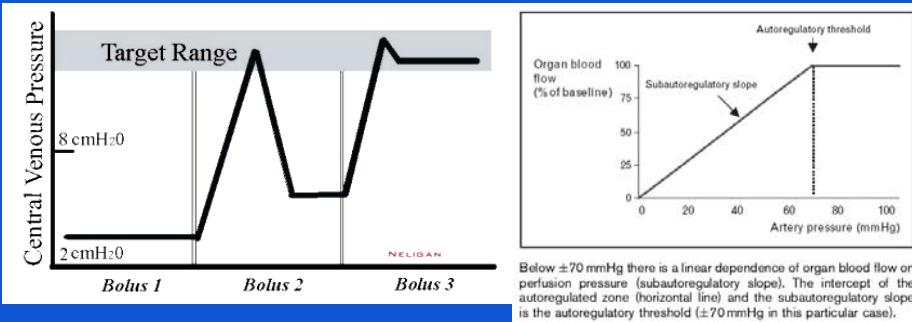
- ❖ 胃肠内气体/液体——IAP增加——IAH/ACS
- ❖ 胃肠减压/灌肠/肛管排气——减少胃肠体积
- ❖ 促胃肠动力药物
 - 红霉素/胃复安/新斯的明
 - 大承气汤
 - 甘露醇
 - 硫酸镁
 - 乳果糖





适当液体平衡

- ❖ 补液是SAP主要治疗措施
- ❖ 避免过度液体治疗
- ❖ 血流动力学监测的目标指导治疗



- Avoid overresuscitation

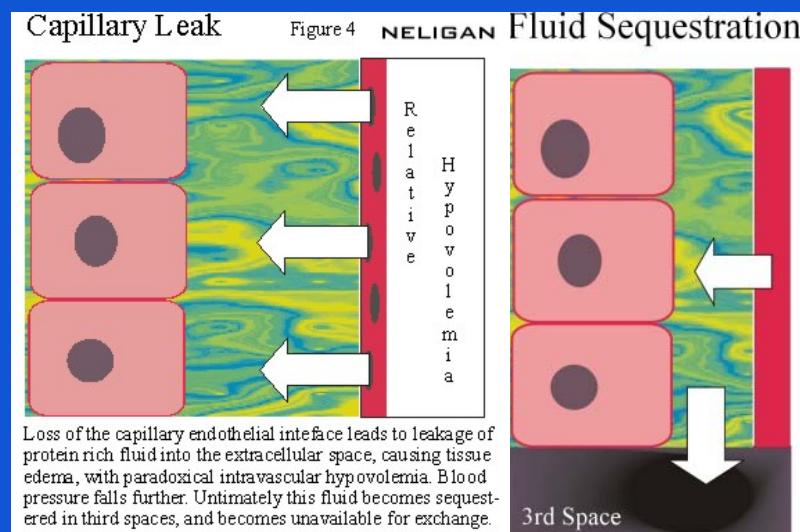
Fluid resuscitation volume should be carefully monitored to avoid over-resuscitation in patients at risk for IAH/ACS (Grade 1B)

Hypertonic crystalloid and colloid-based resuscitation should be considered in patients with IAH to decrease the progression to secondary ACS (Grade 1C)

Adapted from *Intensive Care Medicine* 2006;32(11):1722-1732 & 2007;33(6):951-962

适当液体平衡

❖ 持续静脉-静脉血滤/超滤



SURGICAL TREATMENT OPTIONS

- Immediate decompressive laparotomy reduces IAP and restores systemic perfusion
- Appropriate for patients with ACS refractory to less invasive treatments
- Should not be delayed until organ failure is irreversible



重症急性胰腺炎分期 (severe acute pancreatitis, SAP)

- ❖ 炎症反应期 (<2周)
 - ❖ SIRS→MODS→死亡 (占<20%)
- ❖ 胰腺感染期 (>2-3周)
 - ❖ Sepsis→MODS →死亡 (占>80%)
- ❖ 提高生存率：感染控制

急性胰腺炎（acute pancreatitis, AP）

- ❖ 严重程度
 - ❖ 80-90%为轻型（水肿）——自限性
 - ❖ 10-20%为重型（坏死）——MODS、感染——病死率10-30%
- ❖ 10-35%胰腺坏死并发感染（2-3周）
- ❖ 胰腺坏死感染：重要的死亡危险因素
 - ❖ 病死率：无菌坏死：5-25%；坏死感染：40-50%

Am J Gastroenterol 2006;101:2379–2400
Gastroenterology 2007;133:e1–e25
Am J Surgery 2007;194: S39–S44

胰腺感染诊断

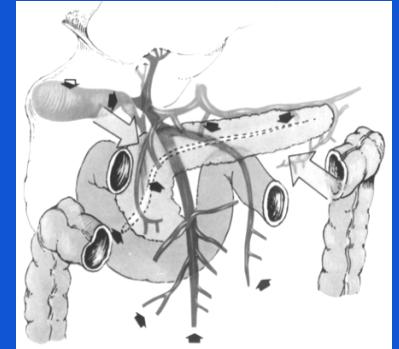
- ❖ 胰腺感染
 - ❖ CT：胰腺坏死，“气泡征”
- ❖ 鉴别无菌和感染性坏死
 - ❖ CT或超声引导下细针穿刺（FNA）
 - ❖ 革兰氏染色和培养
 - ❖ 准确、可靠、安全
 - 敏感性88%，特异性90%

Chin J Dig Dis 2005; 6:47–51

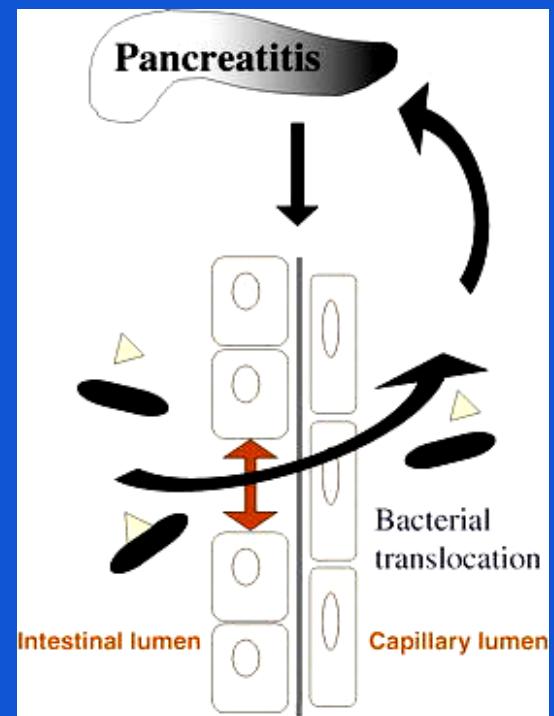
Gut 2005; 54 Suppl 3:iii1–9

Am J Gastroenterol 2006;101:2379–2400

胰腺感染途径



- ❖ 肠源性：屏障↓—肠道细菌移位—感染/MODS
- ❖ 淋巴源性
- ❖ 血源性：导管相关性感染
- ❖ 胆源性
- ❖ 十二指肠：逆行进入主胰管
- ❖ 直接播散



Summary of isolated pathogens in infected pancreatic necrosis

Pathogens	Approximate frequency
Gram-negative rods <i>Enterobacteriaceae (Escherichia coli, Klebsiella spp., Proteus spp.)</i> <i>Pseudomonas aeruginosa</i>	50–70%
Gram-positive cocci <i>Staphylococcus aureus</i> , coagulase-negative staphylococci, <i>Enterococcus</i> spp.	20–40%
Anaerobes <i>Bacteroides</i> spp.	≤ 10%
Fungi <i>Candida</i> spp.	10–40%

预防性抗生素

- ❖ 目的
 - ❖ 预防胰腺感染
 - ❖ 减少手术
 - ❖ 降低病死率?
- ❖ 胰腺组织有效浓度
 - ❖ quinolones (ciprofloxacin, ofloxacin)
 - ❖ carbapenem, imipenem

Pancreatology 2007;7:531–538
Scand J Gastroenterol 2007;42:771–776
Am J Gastroenterol 2008;103:104–110

抗生素评分

<i>Antibiotic</i>	<i>Efficacy factor</i>
Aminoglycosides	
Netilmicin	0.14
Tobramycin	0.12
Acylureidopenicillins	
Mezlocillin	0.71
Piperacillin	0.72
Cephalosporins	
Cefotiam	0.75
Ceftizoxime	0.76
Cefotaxime	0.78
Ceftriaxone	0.79
Quinolones	
Ciprofloxacin	0.86
Oflloxacin	0.87
Carbapenems	
Imipenem	0.98

胰腺组织穿透+覆盖常见感染菌=1.0

Br J Surg 1998; 85:582-587

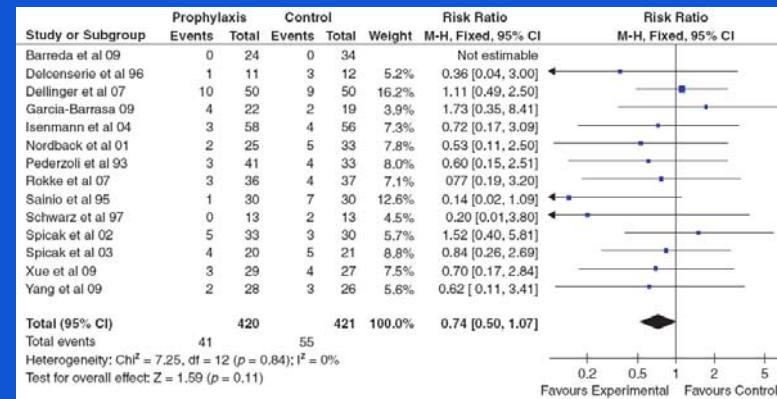


Figure 3. Forest plot of relative risk; [95% confidence intervals]: mortality.

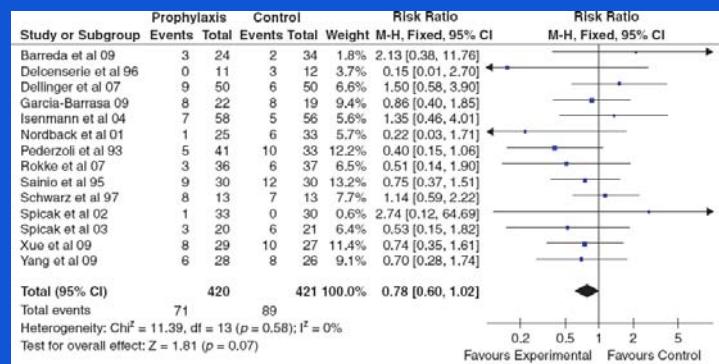


Figure 4. Forest plot of relative risk; [95% confidence intervals]: infected pancreatic necrosis.

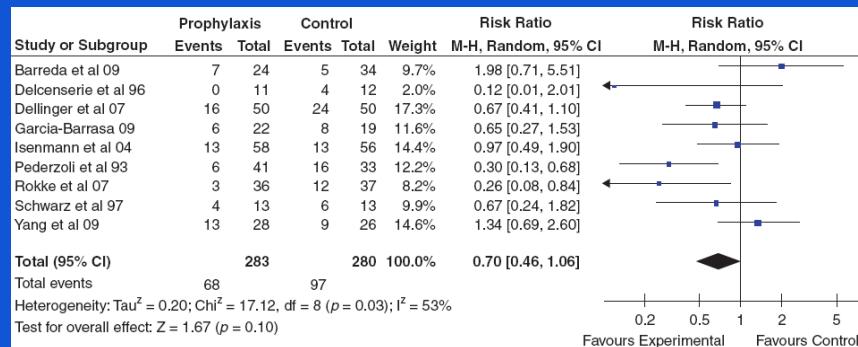


Figure 5. Forest plot of relative risk; [95% confidence intervals]: non-pancreatic infections.

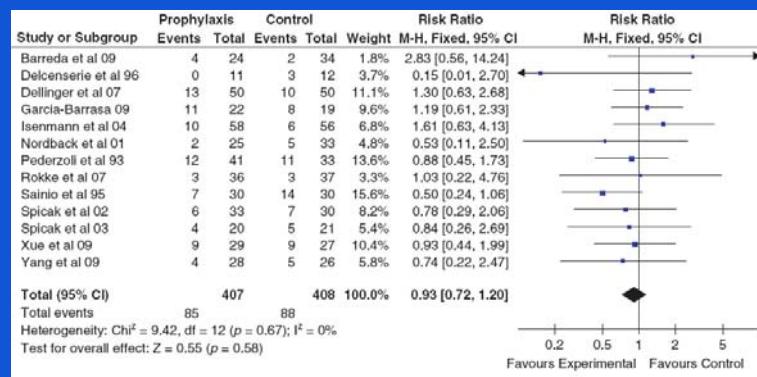


Figure 6. Forest plot of relative risk; [95% confidence intervals]: surgical intervention.

The use of antibiotic prophylaxis was not associated with a statistically significant reduction in mortality, in the incidence of infected pancreatic necrosis, in the incidence of non-pancreatic infections, and in surgical interventions.

预防感染措施

- ❖ 及时、合理液体治疗
 - 改善胰腺灌注减少坏死
 - 24hr内HCT降低<47%
- ❖ 器官功能支持
 - 器官功能不全与胰腺感染互为因果
 - ❖ 避免/减少器官功能不全
 - 缩短器官功能不全持续时间
 - ❖ 持续时间<48hr;或<1w
- ❖ 早期肠内营养
- ❖ 及时控制胆道感染

早期监测与支持治疗

- ❖ 血流动力学监测下/目标指导液体治疗
晶体液、胶体液、去甲肾上腺素/多巴酚丁胺
- ❖ 器官支持——机械通气（PCV/肺保护策略）
改善细胞氧合
- ❖ 促进肠蠕动
改善肠屏障功能、降低腹压
- ❖ 持续血液滤过
液体管理/控制平衡/降低腹压 肾保护? /炎症反应?
- ❖ 早期肠内营养
- ❖ 病因治疗

谢谢！

