Evidence-**B**ased **M**edicine

R1 施秉庚

VS. 王程遠

2008.12.31

Patient Profile

- Name: 董x林
- Gender: male
- Age: 80 years old
- Chart number: 24874229
- Admission date: 2008.10.13

Underlying conditions

- Gastric cancer, grade II adenocarcinoma
- Brongenic adenocarcinoma with metastasis (T4N2M1)
- Obstructive pneumonitis
- Discharge preparation on 12/1

12/2 PM9:00

- S: severe dyspnea with BP drops
- O: BP: 88/40 mmHg, HR: 130, RR:40

  Temp: 39.3 degrees, SpO2: 88%

  Breathing sound: bil. coarse
- A+P: Check whole blood

- WBC: 15300/ul
- CRP: 141.49
- CPK: 144
- CK-MB: 7.2
- TnI: 0.09

Assessment –Dyspnea with BP drops

- Septic shock
- Cardiogenic shock
- Hypovolumic shock
- Neurological shock

Treatment

- Antibiotics: Tazocin 2 vials q8hd
- On CVP
- Vasopressors: Levophed
- Fluid supply: N/S, Gelofusin, FP
- On Foley
- Record I/O

Foreground Questions

Will the use of colloid combined crystalloid have a better outcome than crystalloid alone in septic shock patients?

- Patient/Problem
  - Patients with septic shock
- Intervention
  - Colloid + crystalloid
- Comparison
  - crystalloid
- Outcome
  - mortality rate
- Time
  - Not confined

Summaries

- UpToDate
  - Key words:
    - Septic shock
    - Gelofusin
    - Colloid
  - Article title:
    - **Treatment of severe hypovolemia or hypovolemic shock in adults**
    - **Management of severe sepsis and septic shock in adults**

Treatment of severe hypovolemia or hypovolemic shock in adults

- Colloid versus crystalloid — Both isotonic saline solutions and colloid-containing solutions have been used to replace the extracellular fluid deficit. Some physicians have advocated the administration of a colloid-containing solution (such as albumin or hetastarch) because of two possible advantages over fluid repletion with saline: (1) more rapid plasma volume expansion, since the colloid solution remains in the vascular space (in contrast to saline, two-thirds of which enters the interstitium); and (2) a lesser risk of pulmonary edema, since dilutional hypoalbuminemia will not occur [25].
- However, randomized controlled trials and systematic meta-analyses have failed to demonstrate either of these theoretical benefits [26-34]:
- A well-executed multicenter trial randomly assigned nearly 7000 hypovolemic medical and surgical ICU patients to fluid resuscitation using either 4 percent albumin or normal saline [26]. All-cause mortality at 28 days (the primary end point of the study), multiorgan failure, the duration of hospitalization, and effect upon systemic pH were similar in both groups [35].

- A meta-analysis of 55 studies, published before the above trial, pooled and analyzed data from nearly 3000 critically ill patients randomly assigned to treatment with albumin or crystalloid [33]. There was no evidence for either improved outcome or increased mortality in patients given albumin. Subset analysis identified no group of patients, including those with trauma, burns, hypoalbuminemia, or ascites, that derived statistically significant benefit or harm from albumin transfusion.

Management of severe sepsis and septic shock in adults

- Crystalloid versus colloid — Clinical trials have failed to consistently demonstrate a difference between colloid and crystalloid in the treatment of septic shock [28,29].
- In the saline versus albumin fluid evaluation (SAFE) trial, 6997 critically ill patients were randomly assigned to receive 4 percent albumin or normal saline for up to 28 days [30]. There were no differences between groups for any endpoint, including the primary endpoint, mortality. Among the patients with severe sepsis (18 percent of the total group), there were also no differences in outcome.
- Another randomized trial compared pentastarch (a colloid) to modified Ringer's lactate (a crystalloid) in patients with severe sepsis — the Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP) trial [31]. There was no difference in 28-day mortality, but the trial was stopped early because there was a trend toward increased 90-day mortality among patients who received pentastarch.
- In our clinical practice, we generally use crystalloid because of the higher cost of colloid. We believe that giving a sufficient quantity of intravenous fluids rapidly and targeting appropriate goals is more important than the type of fluid chosen.

Apply the Summary to the Patient

- 4 percent albumin or normal saline (or crystalloid) showed no difference in 28-day mortality rate in septic shock patients

Studies

- Pubmed
  - Key words:
    - colloid
    - Shock
    - crystalloid
  - Article title:
  - Resuscitating patients with early severe sepsis: a Canadian multicentre observational study

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Resuscitating patients with early severe sepsis: a Canadian multicentre observational study

- **Background:** Fluid resuscitation is a key factor in restoring hemodynamic stability and tissue perfusion in patients with severe sepsis. We sought to examine associations of the quantity and type of fluid administered in the first six hours after identification of severe sepsis and hospital mortality, intensive care unit (ICU) mortality, and organ failure.

Methods:

----A retrospective, multicentre cohort study was undertaken at five Canadian tertiary care ICUs. We identified patients with severe sepsis admitted to the ICU between July 1, 2000, and June 30, 2002, using both administrative and clinical databases.

---- Patients were included if they were hypotensive, had an infectious source, and at least two systemic inflammatory response syndrome criteria.

----We recorded total quantity and type of fluid administered for the first six hours after severe sepsis was identified. The first episode of hypotension defined the starting point for collection of fluid data.

----Multivariable regression analyses were performed to examine associations between quantity and type of fluid administered and hospital/ICU mortality, and organ failure.

TABLE I Baseline characteristics

	Entire cohort	*Quantity of fluid (n = 496)*			**Type of Fluid (n = 493)*	
	(n = 496)	*0 – 2 L (n = 210)*	*2 – 4L (n = 186)*	*> 4L (n = 100)*	*Crystalloid (n = 235)*	***Colloid + Crystalloid (n = 258)*
Age mean (SD)	61.8 (16.5)	64.5 (15.7)	60.9 (16.6)	58.0 (17.4)	61.5 (17.3)	62.3 (15.9)
APACHE II** mean (SD)	29.0 (8.0)	28.1 (7.9)	29.2 (8.2)	30.7 (7.6)	28.8 (8.1)	29.2 (7.9)
Sex - females (%, 95% CI)	44.0 (39.5, 48.5)	43.3 (36.5, 50.3)	46.8 (39.4, 54.2)	40.0 (30.3, 50.3)	44.7 (38.2, 51.3)	42.6 (36.5, 48.9)
Type of admission (%, 95% CI)						
Medical	76.1 (72.0, 79.7)	84.8 (79.2, 89.3)	75.3 (68.4, 81.3)	59.0 (48.7, 68.7)	84.3 (79.0, 88.7)	68.2 (62.2, 73.8)
Emergent postoperative	18.3 (15.0, 22.0)	8.6 (5.2, 13.2)	17.7 (12.5, 24.0)	40.0 (30.3, 50.3)	10.6 (7.0, 15.3)	25.6 (20.4, 31.4)
Elective postoperative	5.7 (3.8, 8.1)	6.7 (3.7, 10.9)	7.0 (3.8, 11.7)	1.0 (.03, 5.4)	5.1 (2.7, 8.7)	6.2 (3.6, 9.9)
# Co-morbid diseases (%, 95% CI)						
0	21.6 (18.0, 25.5)	15.2 (10.7, 20.8)	22.6 (16.8, 29.3)	33.0 (23.9, 43.1)	23.0 (17.8, 28.9)	20.5 (15.8, 26.0)
1 – 2	51.2 (46.7, 55.7)	49.1 (42.1, 56.0)	53.2 (45.8, 60.6)	52.0 (41.8, 62.1)	46.8 (40.3, 53.4)	55.0 (48.7, 61.2)
≥ 3	27.2 (23.4, 31.4)	35.7 (29.2, 42.6)	24.2 (18.2, 31.0)	15.0 (8.7, 23.5)	30.2 (24.4, 36.5)	24.4 (19.3, 30.1)
Infectious source (%, 95% CI)						
Pulmonary	37.9 (33.6, 42.3)	47.1 (40.2, 54.1)	35.5 (29.6, 42.8)	23.0 (15.2, 32.5)	39.2 (32.9, 45.7)	37.2 (31.3, 43.4)
Intra-abdominal	30.8 (26.8, 35.1)	23.3 (17.8, 29.7)	29.6 (23.1, 36.7)	49.0 (38.9, 59.2)	21.3 (16.2, 27.1)	39.1 (33.1, 45.4)
Urinary tract	12.1 (10.1, 16.2)	11.4 (7.5, 16.5)	16.7 (11.6, 22.8)	9.0 (4.2, 16.4)	17.4 (12.8, 22.9)	8.9 (5.7, 13.1)
Soft tissue	6.2 (4.3, 8.7)	6.7 (3.7, 11.0)	5.4 (2.6, 9.7)	7.0 (2.9, 13.9)	8.5 (5.3, 12.8)	4.3 (2.1, 7.5)
Other	12.1 (9.4, 15.3)	11.4 (7.5, 16.5)	12.9 (8.5, 18.6)	12.0 (6.4, 20.0)	13.6 (9.5, 18.7)	10.5 (7.0, 14.9)
Vital signs, mean (SD)						
Mean arterial pressure (mmHg)	56.9 (10.2)	58.6 (9.1)	57.0 (8.0)	55.3 (9.3)	57.4 (9.1)	56.0 (11.0)
Heart rate (beats·min^{-1})	107.7 (24.0)	103.5 (25.5)	109.9 (20.6)	112.4 (25.5)	104.3 (23.9)	111.0 (23.7)
Respiratory rate (breaths·min^{-1})	24.2 (9.1)	23.4 (8.7)	24.8 (9.8)	25.0 (8.6)	24.5 (9.0)	24.1 (9.3)
Temperature (degrees Celsius)	37.4 (1.5)	37.4 (1.3)	37.4 (1.6)	37.2 (1.7)	37.2 (1.6)	37.5 (1.3)

TABLE II Fluid data

	Entire cohort	*Quantity of fluid (n = 496)*			**Type of Fluid (n = 493)*	
	(n = 496)	*0 – 2 L (n = 210)*	*2 – 4L (n = 186)*	*> 4L (n = 100)*	*Crystalloid (n = 235)*	***Colloid + Crystalloid (n = 258)*
Total fluid (L) median (IQR)	2.4 (1.4, 3.7)					
Type of fluid (%, 95% CI)						
No fluid	0.6 (0.1, 1.8)	1.4 (0.3, 4.1)	0	0		
Crystalloid alone	47.4 (42.9, 51.9)	58.6 (51.6, 65.3)	44.6 (37.3, 52.1)	29.0 (20.4, 39.0)		
Colloid alone	0	0	0	0		
**Colloid and Crystalloid	52.0 (47.5, 56.5)	40.0 (33.3, 47.0)	55.4 (47.9, 62.6)	71.0 (61.1, 79.6)		
RBC transfusions (%, 95% CI)	12.7 (9.9, 16.0)	6.2 (3.3, 10.3)	11.3 (7.1, 16.7)	29 (20.4, 38.9)	8.5 (5.3, 12.8)	16.7 (12.3, 21.8)
Fresh frozen plasma (%, 95% CI)	0.8 (0.2, 2.0)	0	1.1 (0.1, 3.8)	2.0 (0.2, 7.0)	0.4 (0.0, 2.3)	1.2 (0.0, 3.4)
Platelets (%, 95% CI)	0	0	0	0	0	0

IQR = interquartile range; CI = confidence interval; RBC = red blood cells. *Three patients received no fluid in the first six hours of care; **All colloid use = pentastarch.

Results:

---Of 2,026 potentially eligible patient charts identified, 496 patients met eligibility criteria. The mean age and Acute Physiology and Chronic Health Evaluation score (APACHE II) were 61.8 ± 16.5 yr and 29.0 ± 8.0, respectively.

----No associations between quantity or type of fluid administered and hospital mortality or ICU mortality were identified, and there were no statistically significant associations between quantity or type of fluid administered and organ failure.

----However, more fluid resuscitation was associated with an increased risk of cardiovascular failure [odds ratio (OR) and 95% confidence interval (CI)] for 2–4 L 1.67 (1.03–2.70) and > 4 L 2.34 (1.23–4.44) and a reduced risk of renal failure [OR, 95% CI for 2–4 L 0.48 (0.28–0.83) and > 4 L 0.45 (0.22–0.92)] in the first 24 hr of severe sepsis.

----Administration of colloid and crystalloid fluid as compared to crystalloid fluid alone was associated with a lower risk of renal failure [OR, 95% CI 0.45 (0.26 to 0.76)].

TABLE III Outcomes

	Entire cohort	*Quantity of fluid (n = 496)*			**Type of Fluid (n = 493)*	
	(n = 496)	*0 – 2 L (n = 210)*	*2 – 4L (n = 186)*	*> 4L (n = 100)*	*Crystalloid (n = 235)*	***Colloid + Crystalloid (n = 258)*
Hospital mortality (%, 95% CI)	45.2 (40.7, 49.7)	46.2 (39.3, 53.2)	44.1 (36.8, 51.5)	45.0 (35.0, 55.3)	43.0 (36.6, 49.6)	46.9 (40.7, 53.2)
ICU mortality (%, 95% CI)	34.9 (30.7, 39.2)	31.4 (25.2, 38.2)	35.5 (28.6, 42.8)	41.0 (31.3, 51.3)	30.6 (24.8, 37.0)	38.4 (32.4, 44.6)
Hospital length of stay median (IQR)	14.0 (6.0, 27.0)	14.0 (8.0, 28.0)	13.5 (6.0, 26.0)	17.0 (6.0, 28.0)	13.0 (7.0, 27.0)	15.0 (6.0, 26.0)
ICU length of stay median (IQR)	6.0 (2.0, 12.0)	6.0 (2.0, 11.0)	5.0 (2.0, 12.0)	6.0 (2.0, 12.0)	5.0 (2.0, 11.0)	6.0 (3.0, 12.0)
Organ failure (%, 95% CI) ≥ 2 failed organs	35.3 (31.1, 39.7)	32.4 (26.1, 39.2)	38.2 (31.2, 45.6)	36.0 (26.6, 45.4)	34.9 (28.8, 41.4)	35.66 (29.8, 41.8)

CI = confidence interval; IQR = interquartile range; SOFA = sequential organ failure assessment score. *Three patients required no fluid in the first six hours of care; **All colloid use = pentastarch.

- **Conclusion**: An association between hospital mortality and quantity or type of fluid administered in the first six hours after the diagnosis of severe sepsis was not identifiable. These findings should be considered as hypothesis-generating and warrant confirmation or refutation by randomized controlled trials.

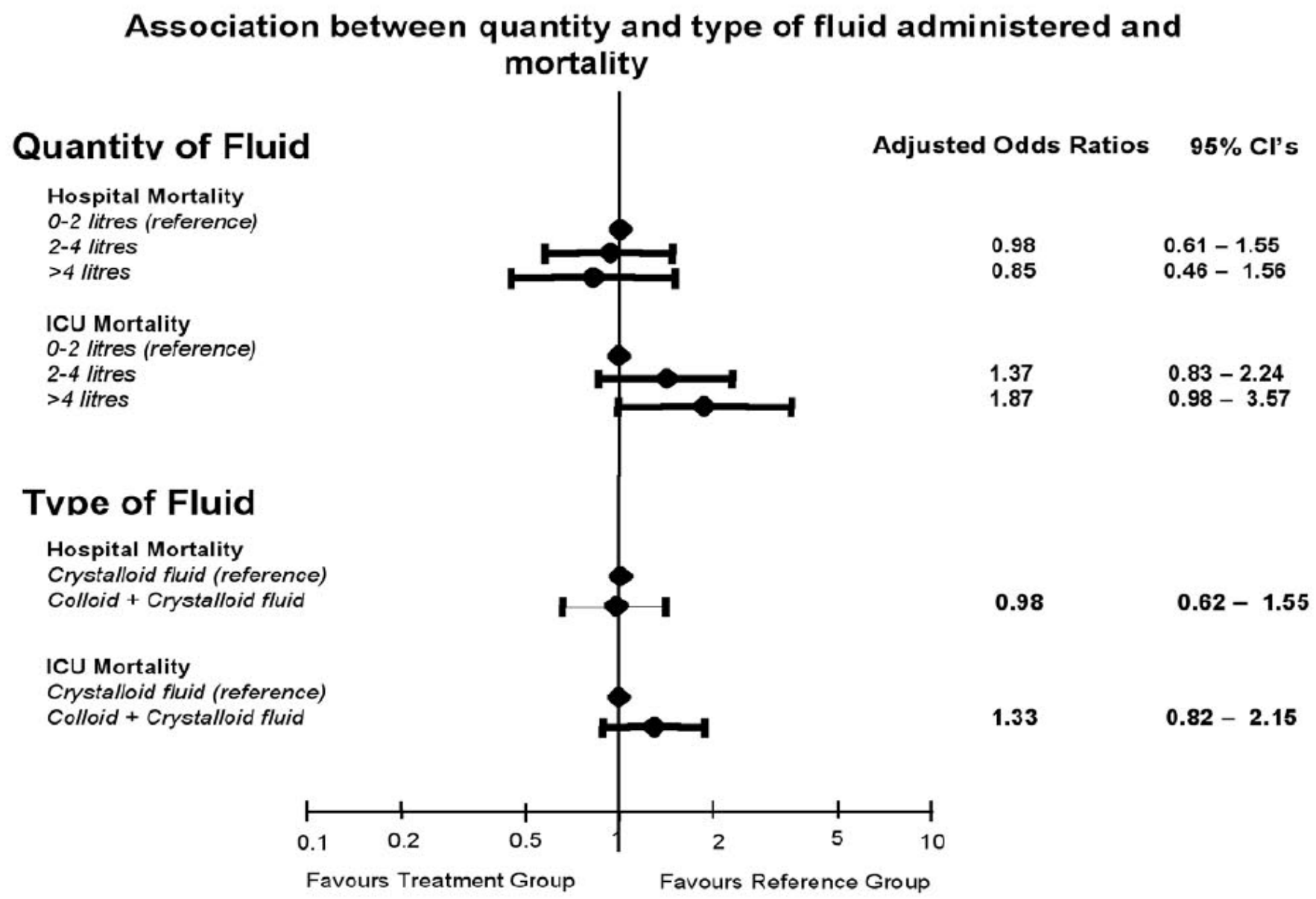

FIGURE Reference group for quantity of fluid = 0–2 L, treatment group = 2–4 and > 4 L. Reference group for type of fluid = crystalloid fluid. Treatment group = colloid and crystalloid fluid. Adjusted odds ratios were generated using multivariable logistic regression that incorporated variables age, sex, Acute Physiology and Chronic Health Evaluation (APACHE II) score, type of admission, infectious source, number of co-morbidities, hospital site, and place in hospital.

Apply the Study to the Patient

- The benefit of colloid and crystalloid fluid as compared to crystalloid fluid alone was of no difference

Appraisal

AAMPICOT

- **A**: Does this paper answer your question?
  Yes.

- **A**:
  - Is the author an expert of the field?
    Yes.
  - Is there any conflict of interest
    No.

Method:證據等級(針對Studies這篇)

Resuscitating patients with early severe sepsis: a Canadian multicentre observational study

Level	與[治療/預防/病因/危害]有關的文獻
1a	用多篇RCT所做成的綜合性分析(SR of RCTs)
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series(poor quality :cohort / case-control studies)
5	沒有經過完整評讀醫學文獻的專家意見

Grades of Recommendation

A	consistent level 1 studies
B	consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies
C	level 4 studies ***or*** extrapolations from level 2 or 3 studies
D	level 5 evidence ***or*** troublingly inconsistent or inconclusive studies of any level

P

- Patients included into the study met one of the following criteria

--- hypotensive, had an infectious source, and at least two systemic inflammatory response syndrome criteria

--- Of 2,026 potentially eligible patient charts identified, 496 patients met eligibility criteria

- Is the population representative of clinical population?
  - It represents a population with severe sepsis and age 61.8±16.5 y/o, APACHE II score 29.0±8.0, female 44%
- Does the selected population been randomized into different categories?
  - No, there is no randomization
  - It was categorized according to their fluid exposure variables
  - There were imbalances among the groups (table I)
  - 0-2L group with age older than >4L group
  - 0-2 L group with less co-morbid illnesses than >4L group

TABLE I Baseline characteristics

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Age mean (SD)	61.8 (16.5)	64.5 (15.7)	60.9 (16.6)	58.0 (17.4)	61.5 (17.3)	62.3 (15.9)
APACHE II** mean (SD)	29.0 (8.0)	28.1 (7.9)	29.2 (8.2)	30.7 (7.6)	28.8 (8.1)	29.2 (7.9)
Sex - females (%, 95% CI)	44.0 (39.5, 48.5)	43.3 (36.5, 50.3)	46.8 (39.4, 54.2)	40.0 (30.3, 50.3)	44.7 (38.2, 51.3)	42.6 (36.5, 48.9)
Type of admission (%, 95% CI)						
Medical	76.1 (72.0, 79.7)	84.8 (79.2, 89.3)	75.3 (68.4, 81.3)	59.0 (48.7, 68.7)	84.3 (79.0, 88.7)	68.2 (62.2, 73.8)
Emergent postoperative	18.3 (15.0, 22.0)	8.6 (5.2, 13.2)	17.7 (12.5, 24.0)	40.0 (30.3, 50.3)	10.6 (7.0, 15.3)	25.6 (20.4, 31.4)
Elective postoperative	5.7 (3.8, 8.1)	6.7 (3.7, 10.9)	7.0 (3.8, 11.7)	1.0 (.03, 5.4)	5.1 (2.7, 8.7)	6.2 (3.6, 9.9)
# Co-morbid diseases (%, 95% CI)						
0	21.6 (18.0, 25.5)	15.2 (10.7, 20.8)	22.6 (16.8, 29.3)	33.0 (23.9, 43.1)	23.0 (17.8, 28.9)	20.5 (15.8, 26.0)
1 – 2	51.2 (46.7, 55.7)	49.1 (42.1, 56.0)	53.2 (45.8, 60.6)	52.0 (41.8, 62.1)	46.8 (40.3, 53.4)	55.0 (48.7, 61.2)
≥ 3	27.2 (23.4, 31.4)	35.7 (29.2, 42.6)	24.2 (18.2, 31.0)	15.0 (8.7, 23.5)	30.2 (24.4, 36.5)	24.4 (19.3, 30.1)
Infectious source (%, 95% CI)						
Pulmonary	37.9 (33.6, 42.3)	47.1 (40.2, 54.1)	35.5 (29.6, 42.8)	23.0 (15.2, 32.5)	39.2 (32.9, 45.7)	37.2 (31.3, 43.4)
Intra-abdominal	30.8 (26.8, 35.1)	23.3 (17.8, 29.7)	29.6 (23.1, 36.7)	49.0 (38.9, 59.2)	21.3 (16.2, 27.1)	39.1 (33.1, 45.4)
Urinary tract	12.1 (10.1, 16.2)	11.4 (7.5, 16.5)	16.7 (11.6, 22.8)	9.0 (4.2, 16.4)	17.4 (12.8, 22.9)	8.9 (5.7, 13.1)
Soft tissue	6.2 (4.3, 8.7)	6.7 (3.7, 11.0)	5.4 (2.6, 9.7)	7.0 (2.9, 13.9)	8.5 (5.3, 12.8)	4.3 (2.1, 7.5)
Other	12.1 (9.4, 15.3)	11.4 (7.5, 16.5)	12.9 (8.5, 18.6)	12.0 (6.4, 20.0)	13.6 (9.5, 18.7)	10.5 (7.0, 14.9)
Vital signs, mean (SD)						
Mean arterial pressure (mmHg)	56.9 (10.2)	58.6 (9.1)	57.0 (8.0)	55.3 (9.3)	57.4 (9.1)	56.0 (11.0)
Heart rate (beats·min^{-1})	107.7 (24.0)	103.5 (25.5)	109.9 (20.6)	112.4 (25.5)	104.3 (23.9)	111.0 (23.7)
Respiratory rate (breaths·min^{-1})	24.2 (9.1)	23.4 (8.7)	24.8 (9.8)	25.0 (8.6)	24.5 (9.0)	24.1 (9.3)
Temperature (degrees Celsius)	37.4 (1.5)	37.4 (1.3)	37.4 (1.6)	37.2 (1.7)	37.2 (1.6)	37.5 (1.3)
Glasgow coma scale score	12.6 (3.4)	12.4 (3.2)	12.9 (3.1)	12.5 (3.4)	12.6 (3.1)	12.5 (3.3)
Place in hospital (%, 95% CI)						
ICU	28.6 (24.9, 32.8)	41.4 (34.7, 48.4)	25.3 (19.2, 32.1)	8.0 (3.5, 15.2)	23.0 (17.8, 28.9)	34.1 (28.3, 40.2)
ER	32.7 (28.6, 37.0)	28.1 (22.1, 34.7)	33.3 (26.6, 40.6)	41.0 (31.2, 51.3)	32.3 (26.4, 38.7)	33.3 (27.6, 39.4)
Hospital ward	16.3 (13.2, 20.0)	16.7 (11.9, 22.4)	18.3 (13.0, 24.6)	12.0 (6.4, 20.0)	16.6 (12.1, 22.0)	15.1 (11.0, 20.1)
OR/PACU	7.1 (5.0, 9.7)	1.4 (0.3, 4.1)	7.5 (4.2, 12.3)	18.0 (11.0, 26.9)	3.0 (1.2, 6.0)	10.8 (7.3, 15.3)
Peripheral hospital	15.3 (12.3, 18.8)	12.4 (8.2, 17.6)	15.6 (10.7, 21.6)	21.0 (13.5, 30.3)	25.1 (19.7, 31.2)	6.6 (3.9, 10.3)
# Days in hospital (before Identification of severe sepsis) Median (IQR)	0 (0, 2)	1 (0, 3)	0 (0, 2)	0 (0, 1)	0 (0, 2)	1 (0, 3)

CI = confidence interval; ICU = intensive care unit; ER = emergency room; OR = operating room; PACU = postoperative care unit; # =

I

- Colloid + crystalloid

- ✓ Appraisal
- ✓ Treatment pathway: peripheral vs. central
- ✓ Frequency: continuous vs. intermittent
- ✓ Type of fluid: N/S vs. L/R vs. Gelofusin vs. Albumin

C

- Crystalloid

- ✓ Appraisal
- ✓ Treatment pathway: peripheral vs. central
- ✓ Frequency: continuous vs. intermittent
- ✓ Type of fluid: N/S vs. L/R

O

- Primary analysis
  - No associations between quantity or type of fluid administered and hospital mortality or ICU mortality were identified
- Secondary analysis
  - there were no statistically significant associations between quantity or type of fluid administered and organ failure

- Crystalloid group with higher emergent postoperative rate than combined group
- Combined group with higher intraabdominal infection rate than crystalloid group
- Crystalloid group with higher peripheral hospital rate than combined group
- Individual duration in ICU (not mentioned)

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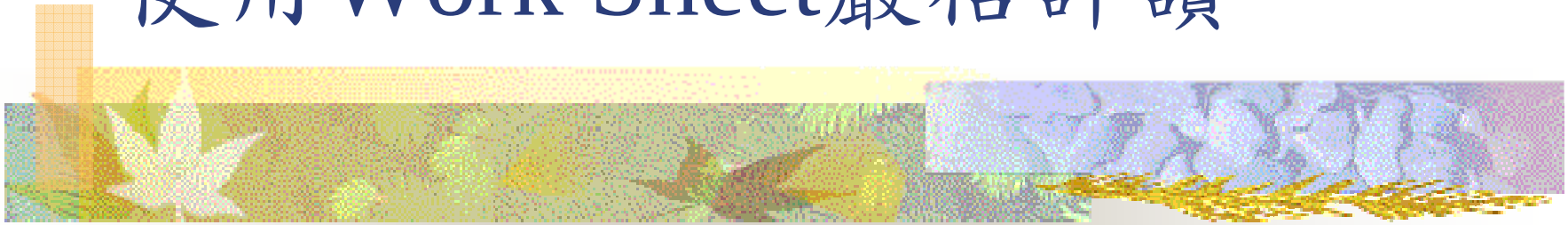
Medical	76.1 (72.0, 79.7)	84.8 (79.2, 89.3)	75.3 (68.4, 81.3)	59.0 (48.7, 68.7)	84.3 (79.9, 88.7)	68.2 (62.3, 73.8)
Emergent postoperative	18.3 (15.0, 22.0)	8.6 (5.2, 13.2)	17.7 (12.5, 24.0)	40.0 (30.3, 50.3)	10.6 (7.0, 15.3)	25.6 (20.4, 31.4)
Elective postoperative	5.7 (3.8, 8.1)	6.7 (3.7, 10.9)	7.0 (3.8, 11.7)	1.0 (.03, 5.4)	5.1 (2.7, 8.7)	6.2 (3.6, 9.9)
# Co-morbid diseases (%, 95% CI)						
0	21.6 (18.0, 25.5)	15.2 (10.7, 20.8)	22.6 (16.8, 29.3)	33.0 (23.9, 43.1)	23.0 (17.8, 28.9)	20.5 (15.8, 26.0)
1 – 2	51.2 (46.7, 55.7)	49.1 (42.1, 56.0)	53.2 (45.8, 60.6)	52.0 (41.8, 62.1)	46.8 (40.3, 53.4)	55.0 (48.7, 61.2)
≥ 3	27.2 (23.4, 31.4)	35.7 (29.2, 42.6)	24.2 (18.2, 31.0)	15.0 (8.7, 23.5)	30.2 (24.4, 36.5)	24.4 (19.3, 30.1)
Infectious source (%, 95% CI)						
Pulmonary	37.9 (33.6, 42.3)	47.1 (40.2, 54.1)	35.5 (29.6, 42.8)	23.0 (15.2, 32.5)	39.2 (32.9, 45.7)	37.2 (31.3, 43.4)
Intra-abdominal	30.8 (26.8, 35.1)	23.3 (17.8, 29.7)	29.6 (23.1, 36.7)	49.0 (38.9, 59.2)	21.3 (16.2, 27.1)	39.1 (33.1, 45.4)
Urinary tract	12.1 (10.1, 16.2)	11.4 (7.5, 16.5)	16.7 (11.6, 22.8)	9.0 (4.2, 16.4)	17.4 (12.8, 22.9)	8.9 (5.7, 13.1)
Soft tissue	6.2 (4.3, 8.7)	6.7 (3.7, 11.0)	5.4 (2.6, 9.7)	7.0 (2.9, 13.9)	8.5 (5.3, 12.8)	4.3 (2.1, 7.5)
Other	12.1 (9.4, 15.3)	11.4 (7.5, 16.5)	12.9 (8.5, 18.6)	12.0 (6.4, 20.0)	13.6 (9.5, 18.7)	10.5 (7.0, 14.9)
Vital signs, mean (SD)						
Mean arterial pressure (mmHg)	56.9 (10.2)	58.6 (9.1)	57.0 (8.0)	55.3 (9.3)	57.4 (9.1)	56.0 (11.0)
Heart rate (beats·min^{-1})	107.7 (24.0)	103.5 (25.5)	109.9 (20.6)	112.4 (25.5)	104.3 (23.9)	111.0 (23.7)
Respiratory rate (breaths·min^{-1})	24.2 (9.1)	23.4 (8.7)	24.8 (9.8)	25.0 (8.6)	24.5 (9.0)	24.1 (9.3)
Temperature (degrees Celsius)	37.4 (1.5)	37.4 (1.3)	37.4 (1.6)	37.2 (1.7)	37.2 (1.6)	37.5 (1.3)
Glasgow coma scale score	12.6 (3.4)	12.4 (3.2)	12.9 (3.1)	12.5 (3.4)	12.6 (3.1)	12.5 (3.3)
Place in hospital (%, 95% CI)						
ICU	28.6 (24.9, 32.8)	41.4 (34.7, 48.4)	25.3 (19.2, 32.1)	8.0 (3.5, 15.2)	23.0 (17.8, 28.9)	34.1 (28.3, 40.2)
ER	32.7 (28.6, 37.0)	28.1 (22.1, 34.7)	33.3 (26.6, 40.6)	41.0 (31.2, 51.3)	32.3 (26.4, 38.7)	33.3 (27.6, 39.4)
Hospital ward	16.3 (13.2, 20.0)	16.7 (11.9, 22.4)	18.3 (13.0, 24.6)	12.0 (6.4, 20.0)	16.6 (12.1, 22.0)	15.1 (11.0, 20.1)
OR/PACU	7.1 (5.0, 9.7)	1.4 (0.3, 4.1)	7.5 (4.2, 12.3)	18.0 (11.0, 26.9)	3.0 (1.2, 6.0)	10.8 (7.3, 15.3)
Peripheral hospital	15.3 (12.3, 18.8)	12.4 (8.2, 17.6)	15.6 (10.7, 21.6)	21.0 (13.5, 30.3)	25.1 (19.7, 31.2)	6.6 (3.9, 10.3)
# Days in hospital (before Identification of severe sepsis) Median (IQR)	0 (0, 2)	1 (0, 3)	0 (0, 2)	0 (0, 1)	0 (0, 2)	1 (0, 3)

CI = confidence interval; ICU = intensive care unit; ER = emergency room; OR = operating room; PACU = postoperative care unit; # = number; IQR = interquartile range. *Three patients received no fluid in the first six hours of care; **All colloid use = pentastarch.

使用Work Sheet嚴格評讀



Cohort 12-questions

1 Did the study address a clearly focused issue? *HINT: A question can be focused in terms of:* *- the population studied* *- the risk factors studied* *- the outcomes considered* *- is it clear whether the study tried to detect a beneficial or harmful effect?*	**Yes** ❑	**Can't tell** ❑	**No** ❑
2 Did the authors use an appropriate method to answer their question? *HINT: Consider* *- Is a cohort study a good way of answering the question under the circumstances?*	**Yes** ❑	**Can't tell** ❑	**No** ❑
3 Was the cohort recruited in an acceptable way? *HINT: We are looking for selection bias which might compromise the generalisability of the findings:* *- Was the cohort representative of a defined population?* *- Was there something special about the cohort?* *- Was everybody included who should have been included?*	**Yes** ❑	**Can't tell** ❑	**No** ❑

RCT may be better than Cohort study

Focus on ICU patient

4. Was the exposure accurately measured to minimize bias? *HINT: We are looking for measurement or classification bias:* - *Did they use subjective or objective measurements?* - *Do the measures truly reflect what you want them to (have they been validated)?* - *Were all the subjects classified into exposure groups using the same procedure?*	**Yes** ❑	**Can't tell** ❑	**No** ❑
	Intervention was not definitely defined in route, etc.		
5. Was the outcome accurately measured to minimize bias? *HINT: We are looking for measurement or classification bias:* - *Did they use subjective or objective measurements?* - *Do the measures truly reflect what you want them to (have they been validated)?* - *Has a reliable system been established for detecting all the cases (for measuring disease occurrence)?* - *Were the measurement methods similar in the different groups?* - *Were the subjects and/or the outcome assessor blinded to exposure (does this matter)?*	**Yes** ❑	**Can't tell** ❑	**No** ❑
	Outcome was defined by organ failure not laboratory data		
6. A. Have the authors identified all important confounding factors? **List the ones you think might be important, that the authors missed.**	**Yes** ❑	**Can't tell** ❑	**No** ❑
	No data of vasopressor noted		
B. Have they taken account of the confounding factors in the design and/or analysis?	**Yes** ❑	**Can't tell** ❑	**No** ❑

8. What are the results of this study?

HINT:

- *What are the bottom line results?*
- *Have they reported the rate or the proportion between the exposed/unexposed, the ratio/the rate difference?*
- *How strong is the association between exposure and outcome (RR,)?*
- *What is the absolute risk reduction (ARR)?*

No associations between quantity or type of fluid administered and hospital mortality or ICU mortality were identified

9. How precise are the results?

How precise is the estimate of the risk?

HINT:

- *Size of the confidence intervals*

10. Do you believe the results?

HINT:

- *Big effect is hard to ignore!*
- *Can it be due to bias, chance or confounding?*
- *Are the design and methods of this study sufficiently flawed to make the results unreliable?*
- *Consider Bradford Hills criteria (eg time sequence, dose-response gradient, biological plausibility, consistency).*

Results only partly believed due to many bias noted

Yes	Can't tell	No
❑	❑	❑

11. Can the results be applied to the local population? *HINT: Consider whether* - *The subjects covered in the study could be sufficiently different from your population to cause concern.* - *Your local setting is likely to differ much from that of the study* - *Can you quantify the local benefits and harms?*	**Yes** ❑	**Can't tell** ❑	**No** ❑
	A part of population of pulmonary infection P't was not completely monitored in ICU		
12. Do the results of this study fit with other available evidence?	**Yes** ❑	**Can't tell** ❑	**No** ❑
	Similar to results in Up to Date		

Apply-臨床應用

將study的結果應用在病人身上

Patient:

Similar: septic shock patients

Differences:

---a part population of pulmonary infection

---low ratio of patient of hospital ward

Intervention & Compare:

Similar: crystalloid vs. combined

Differences:

---N/S + Gelofusin vs. Pentastarch + crystalloid

---route of infusion and frequency

---under CVP monitor (?)

Outcome:

Differences:

---bias between several subgroups

總結與討論

- 結論:Colloid + crystalloid無法比單獨使用crystalloid有較佳之癒後，因此不需要使用較貴之Colloid 。
- 但是

  --肺部感染只占一定比例

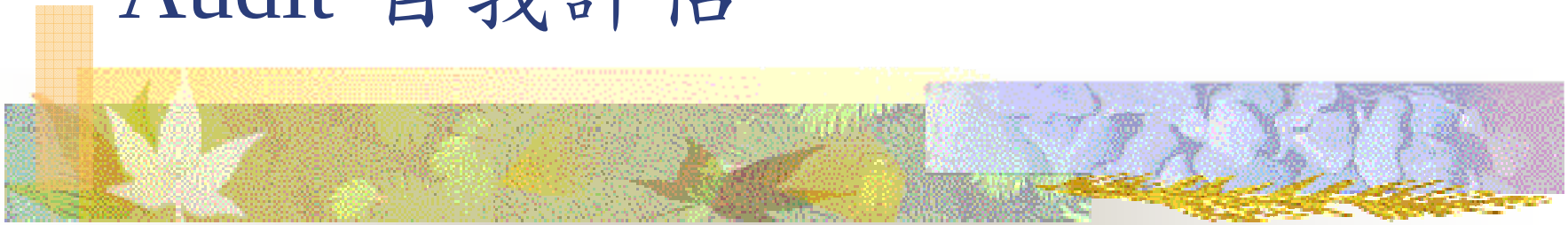
  --並非所有的病人都需要進ICU

  --雖為crystalloid和Colloid + crystalloid比較 即使是crystalloid之間也有所不同
- 總結:

  --和其他資訊相同

  --仍需更進一步RCT

Audit-自我評估



在「提出臨床問題」方面的自我評估

- 我提出的問題是否具有臨床重要性？有，因為可決定何種fluid較佳。
- 我是否明確的陳述了我的問題？
  - 我的foreground question 是否可以清楚的寫成PICO？可
  - 我的background question是否包括what, when, how, who等字根？有，但未全能概括
- 我是否清楚的知道自己問題的定位？（亦即可以定位自己的問題是屬於診斷上的、治療上的、預後上的或流行病學上的），並據以提出問題？知道，屬於治療範疇
- 對於無法立刻回答的問題，我是否有任何方式將問題紀錄起來以備將來有空時再找答案？有

在「搜尋最佳證據」方面的自我評估

- 我是否已盡全力搜尋？是(?)
- 我是否知道我的問題的最佳證據來源？是
- 我是否從大量的資料庫來搜尋答案？是
- 我工作環境的軟硬體設備是否能支援我在遇到問題時進行立即的搜尋？是，學校買的版權資源非常便利，但有些paper全文仍無法取得
- 我是否在搜尋上愈來愈熟練了？是
- 我會使用「斷字」、布林邏輯、同義詞、MeSH term，限制(limiters)等方法來搜尋？部份會
- 我的搜尋比起圖書館人員或其他對於提供病人最新最好醫療有熱情的同事如何？普通程度吧

關於「嚴格評讀文獻」方面的自我評估

- 我是否盡全力做評讀了？盡力而為，但仍有不了解的項目
- 我是否了解Number need to treat 的意義？約略了解
- 我是否了解Likelihood Ratios的意義？約略了解
- 我是否了解worksheet每一項的意義？不太了解
- 評讀後，我是否做出了結論？yes

關於「應用到病人身上」的自我評估

- 我是否將搜尋到的最佳證據應用到我的臨床工作中？是
- 我是否能將搜尋到的結論如NNT, LR用病人聽得懂的方式解釋給病人聽？還不可以
- 當搜尋到的最佳證據與實際臨床作為不同時，我如何解釋？目前無不同，故暫不需解釋

改變「醫療行為」的自我評估

- 當最佳證據顯示目前臨床策略需改變時，我是否遭遇任何阻止改變的阻力？
  沒有，目前證據未改變臨床策略
- 我是否因此搜尋結果而改變了原來的治療策略？做了那些改變？沒有改變

效率評估

- 這篇報告，我總共花了多少時間？四天
- 我是否覺得這個進行實證醫學的過程是值得的？值得
- 我還有那些問題或建議？評讀paper的方法不甚熟練