CQ 12–3 敗血症患者では経腸栄養をいつ始めるか？

検索データベース
■ MEDLINE (PubMed/Ovid)
■ CENTRAL
■ 医学中央雑誌
□ その他（ ）

検索式とヒット数
PubMed search strategy（検索日 31年 4月 30日）

| #1 | (((((((("Sepsis"[Mesh] or "Sepsis"[tiab] or "critical illness"[Mesh] or "critical illness"[tiab]) or (seps*[tiab] OR septicem*[tiab] OR septicaem*[tiab] OR "blood stream infection"[tiab] OR endotox*[tiab]) or ("Systemic Inflammatory Response Syndrome"[Mesh] OR "Systemic Inflammatory Response Syndrome"[tiab] OR "SIRS"[tiab]) or ("Critical Illness"[Mesh] OR "Critical Care"[Mesh] OR "Intensive Care Units"[Mesh] OR stressed[tiab] OR "critically ill"[tiab] OR "critical care"[tiab] OR "intensive care"[tiab] OR "acute disease"[Mesh] or "acute disease"[tiab]) or ("Respiration, Artificial"*[Mesh] or "Respiration"*[Mesh] OR "Respiration, Artificial"*[tiab] OR "Postoperative Care" )))))))) | 763149 |
| #2 | (((("enteral nutrition"[MeSH] OR "enteral nutrition"[tiab]))) | 21896 |
| #3 | "Time Factors"[Mesh] or "Energy intake"[Mesh] | 1190931 |
| #4 | ((((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals [mh] NOT humans [mh]))) | 3888733 |
| #5 | #1 and #2 and #3 and #4 | 508 |

CENTRAL search strategy（検索日 31年 4月 22日）

| ID | Search                                      | Hits  |
|----|---------------------------------------------|-------|
| #1 | MeSH descriptor: [Sepsis] explode all trees | 3998  |
#2 (Sepsis):ti,ab,kw

#3 MeSH descriptor: [Critical Illness] explode all trees

#4 (critical illness):ti,ab,kw

#5 (seps*):ti,ab,kw

#6 (septicem*):ti,ab,kw

#7 (septicaem*):ti,ab,kw

#8 (blood stream infection):ti,ab,kw

#9 (endotoxi*):ti,ab,kw

#1 MeSH descriptor: [Systemic Inflammatory Response Syndrome] explode all trees

1020

1

1

1

MeSH descriptor: [Critical Illness] explode all trees

1845
(Critical Illness):ti,ab,kw 3785

MeSH descriptor: [Critical Care] explode all trees 1918

("critical care"):ti,ab,kw 3515

MeSH descriptor: [Intensive Care Units] explode all trees 3260

(Intensive Care Units):ti,ab,kw 5825

(stressed):ti,ab,kw 958

(critically ill):ti,ab,kw 5980

("critical care"):ti,ab,kw 3515

(intensive care):ti,ab,kw 2508
MeSH descriptor: [Acute Disease] explode all trees 9257

(acute disease):ti,ab,kw 4112

MeSH descriptor: [Respiration, Artificial] explode all trees 5721

(Respiration, Artificial*):ti,ab,kw 3431

MeSH descriptor: [Postoperative Care] explode all trees 4290

("postoperative care"):ti,ab,kw 7842

MeSH descriptor: [Enteral Nutrition] explode all trees 1713

(enteral nutrition):ti,ab,kw 4413

MeSH descriptor: [Time Factors] explode all trees 6206
医学中央雑誌 search strategy (検索日 31年 4月 22日)

| #1 | 効血性/TH or 効血性/TA or ショック-効血症性/TH or ショック-効血症性/TA and PT=会議録除く | 22405 |
|----|--------------------------------------------------------------------------------|-------|
| #2 | 菌血症/TH or 菌血症/TA or 内毒素/TH or エンドトキシン/TA or 血流感染/TA and PT=会議録除く | 13642 |

#3 (Time Factors):ti,ab,kw

#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

#3 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20

#3 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28

#3

#29 or #30

#3

MeSH descriptor: [Energy Intake] explode all trees

#3

("energy intake"):ti,ab,kw
| # | 全身性炎症反応症候群/TH or 全身性炎症反応症候群/TA or SIRS/TA and PT=会議録除く | 17956 |
|---|---|---|
| #4 | 多臓器不全/TH or 多臓器不全/TA or MOF/TA and PT=会議録除く | 7425 |
| #5 | ICU/TH or ICU/TA or クリティカルケア/TH or 集中治療/TA or ストレス/TH or ストレス/TA or 侵襲/TA and PT=会議録除く | 156287 |
| #6 | 膵炎/TH or 膵炎/TA or 熱傷/TH or 熱傷/TA or 創傷と損傷/TH or 創傷と損傷/TA and PT=会議録除く | 218821 |
| #7 | #1 or #2 or #3 or #4 or #5 or #6 | 396414 |
| #8 | 経腸栄養/TH or 経腸栄養/TA and PT=会議録除く | 12420 |
| #9 | ランダム化比較試験/TH or 準ランダム化比較試験/TH or ランダム化/AL or 無作為化/AL or 比較試験/AL or 臨床試験/AL or プラセボ/AL or 対照/AL or コントロール/AL or 臨床研究/AL | 301704 |
| #10 | #7 and #8 and #9 | 196 |
# Overall Mortality

**Study or Subgroup** | **Early EN** | **Delayed EN** | **Total** | **Weight** | **Risk Ratio** | **Risk Ratio** | **Risk of Bias** | **A** | **B** | **C** | **D** | **E**
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
Chiarelli1990 | 0 | 10 | 0 | 10 | Not estimable | | | | | | | |
Chaudhri2012 | 2 | 25 | 3 | 34 | 5.7% | 0.91 [0.16, 5.63] | | | | | | |
Eyer1993 | 2 | 19 | 2 | 19 | 4.9% | 1.00 [0.16, 6.38] | | | | | | |
Kampani1999 | 0 | 14 | 1 | 14 | 1.7% | 0.33 [0.01, 7.51] | | | | | | |
Kampani2004 | 0 | 27 | 1 | 25 | 1.7% | 0.31 [0.01, 7.26] | | | | | | |
Malhotra2004 | 12 | 100 | 16 | 100 | 34.5% | 0.75 [0.37, 1.50] | | | | | | |
Moses2009 | 3 | 29 | 3 | 30 | 7.3% | 1.03 [0.23, 4.71] | | | | | | |
Nguyen2012 | 4 | 14 | 4 | 14 | 12.2% | 1.00 [0.31, 3.23] | | | | | | |
Peck2004 | 4 | 14 | 4 | 13 | 14.4% | 0.74 [0.25, 2.18] | | | | | | |
Petrov2013 | 0 | 17 | 0 | 18 | Not estimable | | | | | | | |
Pupelis2001 | 1 | 30 | 7 | 30 | 4.0% | 0.14 [0.02, 1.99] | | | | | | |
Singh1998 | 4 | 21 | 4 | 22 | 10.7% | 1.05 [0.30, 3.66] | | | | | | |
Sun2013 | 2 | 30 | 1 | 30 | 3.0% | 2.60 [0.19, 20.90] | | | | | | |
**Total (95% CI)** | 350 | 359 | 0 | 100.0% | 0.79 [0.52, 1.19] | | | | | | |
**Total events** | 34 | 47 | | | | | | | | | | |
**Heterogeneity** | Tau² = 0.00; Ch² = 4.64, df = 10 (P = 0.91); I² = 0% | | | | | | | | | | | |
**Test for overall effect** | Z = 1.13 (P = 0.26) | | | | | | | | | | | |

**Risk of bias legend**
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Incomplete outcome data (attrition bias)
- (D) Selective reporting (reporting bias)
- (E) Other bias

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### Forest Plot

- SE(log(RR))
- RR
- 0.01
- 0.1
- 1
- 10
- 100
- 0.5
- 1
- 1.5
- 2
- 0.5

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**Favours [Experimental]**
- **Favours [Control]**
ICU Mortality

| Study or Subgroup | Early EN Events | Delayed EN Events Total | Weight | Risk Ratio M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI | Risk of Bias |
|-------------------|----------------|------------------------|--------|--------------------------------|--------------------------------|---------------|
| Chiarelli1990     | 0              | 10                     | 10     | Not estimable                  |                                |               |
| Chouvardakis2012  | 2              | 25                     | 14     | 0.91 [0.16, 5.03]              |                                |               |
| Eyre1993          | 2              | 19                     | 19     | 4.93 [0.94, 24.91]             |                                |               |
| Kamps1999         | 0              | 14                     | 14     | 0.33 [0.01, 7.55]              |                                |               |
| Kampani2004       | 0              | 27                     | 27     | 1.31 [0.01, 17.26]             |                                |               |
| Malhotra2004      | 12             | 100                    | 100    | 34.5% [0.75, 1.75]             |                                |               |
| Moses2009         | 3              | 29                     | 30     | 7.3% [0.35, 4.71]              |                                |               |
| Nguyen2002        | 4              | 14                     | 14     | 12.2% [0.31, 3.23]             |                                |               |
| Peck2004          | 4              | 14                     | 13     | 14.4% [0.74, 2.18]             |                                |               |
| Petrovic2013      | 0              | 17                     | 18     | Not estimable                  |                                |               |
| Pupelis2001       | 1              | 30                     | 30     | 4.0% [0.14, 1.06]              |                                |               |
| Singh1998         | 4              | 21                     | 22     | 10.7% [0.30, 3.66]             |                                |               |
| Sun2013           | 2              | 30                     | 30     | 3.0% [2.00, 2.90]              |                                |               |

Total (95% CI) 350
Total events 47

Heterogeneity: 0.40, 4.64, df=10 (P = 0.91); 0.0%
Test for overall effect: Z = 1.13 (P = 0.26)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Incomplete outcome data (attrition bias)
(D) Selective reporting (reporting bias)
(E) Other bias

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The legend for the risk of bias is as follows:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Incomplete outcome data (attrition bias)
(D) Selective reporting (reporting bias)
(E) Other bias

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The graph shows the funnel plot with SE(log(RR)) on the y-axis and RR on the x-axis.
## Hospital Mortality

| Study or Subgroup | Early EN Events Total | Delayed EN Events Total | Weight | Risk Ratio M-H, Random, 95% CI |
|-------------------|-----------------------|-------------------------|--------|------------------------------|
| Petrov2013        | 0 17                  | 0 18                    |        | Not estimable                |
| Sun2013           | 2 30                  | 1 30                    | 100.0% | 2.00 [0.19, 20.90]           |
| Total events      | 47                    | 48                      | 100.0% | 2.00 [0.19, 20.90]           |

Heterogeneity: Not applicable

Test for overall effect: $Z = 0.38$ ($P = 0.56$)
### ICU stay

| Study or Subgroup | Early EN | Mean | SD | Total | Mean | SD | Total | Weight | Mean Difference | V% Random, 95% CI | Risk of Bias |
|-------------------|----------|------|----|-------|------|----|-------|--------|-----------------|------------------|--------------|
| Jay et al. 1993   | 11.8     | 7.9  | 15 | 8.9   | 6.7  | 19 | 20.8% | 1.50   | 1.90 [-2.76, 6.26] | +                | 1 2 3 4 5 |
| Kompan et al. 1999| 15.4     | 11.7 | 14 | 13.7  | 10.5 | 14 | 13.7% | 1.70   | -6.33, 9.93      | -                | 1 2 3 4 5 |
| Kompan et al. 2004| 15.9     | 9.7  | 27 | 20.6  | 18.5 | 25 | 13.5% | -4.70  | -12.82, 3.42     | -                | 1 2 3 4 5 |
| Nguyen et al. 2012| 15.9     | 1.9  | 14 | 11.3  | 0.8  | 14 | 27.4% | 4.46   | 3.32, 5.68       | -                | 1 2 3 4 5 |
| Pecic et al. 2004  | 40       | 32   | 14 | 37    | 33   | 13 | 2.7%  | 3.60   | 21.55, 27.55      | -                | 1 2 3 4 5 |
| Sun et al. 2013   | 9.35     | 7    | 30 | 13.7  | 10.1 | 30 | 21.3% | -4.37  | 8.77, 0.03        | -                | 1 2 3 4 5 |
| **Total (95% CI)**| 11.8     | 7.9  | 115| 13.7  | 10.1 | 30 | 21.3% | 0.38   | [-3.89, 4.65]     | -                | 1 2 3 4 5 |

**Test for overall effect:** Z = 0.17 (P = 0.86)  
**Heterogeneity:** Tau^2 = 17.95; CH^2 = 20.47; df = 5 (P = 0.001); I^2 = 78%

**Risk of bias legend:**  
(A) Random sequence generation (selection bias)  
(B) Allocation concealment (selection bias)  
(C) Incomplete outcome data (attrition bias)  
(D) Other bias
## Hospital Stay

| Study or Subgroup | Early EN | Delayed EN | Mean Difference | Risk of Bias |
|-------------------|----------|------------|----------------|--------------|
| Chalmers2000      | 68.2     | 10.4       | 10 89 18.9     | 10 4.8% -18.9% [-33.37, -6.63] | ★ ★ ★ ★ ★ |
| Moorse2000        | 14.8     | 8.2        | 29 11.5 5.8    | 30 26.1% 3.30 [-0.34, 6.94] | ★ ★ ★ ★ ★ |
| Ferro2013         | 9        | 5.7        | 17 8.5 5.6     | 18 23.0% 6.50 [-9.23, 2.43] | ★ ★ ★ ★ ★ |
| Popplete2001      | 35.3     | 22.9       | 30 35.8 34.5   | 30 4.3% -0.50 [-14.73, 13.73] | ★ ★ ★ ★ ★ |
| Singh2000         | 14       | 1.5        | 21 13 1.5      | 22 35.2% 1.00 [0.00, 2.00] | ★ ★ ★ ★ ★ |

Total (95% CI): 107 11.0 100.0% 0.43 [-2.71, 3.53]

**Heterogeneity Test:** Tau² = 6.23; CH² = 10.05, df = 4 (P = 0.03); I² = 63%

**Test for overall effect:** Z = 0.26 (P = 0.80)

### Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Incomplete outcome data (attrition bias)
- (D) Selective reporting (reporting bias)
- (E) Other bias

### Test of MD (Mean Difference)

| MD | Early EN | Delayed EN | SE(MD) |
|----|----------|------------|--------|
| -20| -10      | 0          | 10     |
| -10| -5       | 0          | 5      |
| 0  | 0        | 0          | 0      |
| 5  | 10       | 0          | 2      |
| 10 | 15       | 0          | 4      |
| 15 | 20       | 0          | 6      |
Any infection

| Study or Subgroup | Early EN Events | Delayed EN Events | Total Events | Weight | M-H Random, 95% CI | Risk Ratio M-H Random, 95% CI | Risk of Bias |
|-------------------|-----------------|-------------------|--------------|--------|-------------------|--------------------------|--------------|
| Eyer1993          | 8               | 19                | 27           | 31.8%  | 2.00 [0.72, 5.33] | 1.00 [0.38, 2.63]         | A             |
| Moses2009         | 14              | 29                | 43           | 68.2%  | 0.97 [0.57, 1.67] | 1.00 [0.62, 1.69]         | B            |
| Total             | 22              | 49                | 71           | 100.0% | 1.22 [0.62, 2.39] | 1.00 [0.62, 2.39]         | C,D,E        |

Heterogeneity: Tau² = 0.10; CH² = 1.61, df = 1 (P = 0.20); I² = 36%

Test for overall effect: Z = 0.37 (P = 0.70)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Incomplete outcome data (attrition bias)
(D) Selective reporting (reporting bias)
(E) Other bias
Pneumonia

| Study or Subgroup | Early EN | Delayed EN | Risk Ratio | Risk of Bias |
|-------------------|----------|------------|------------|--------------|
|                   | Events   | Total      | Weight     | M-H, Random, 95% CI | M-H, Random, 95% CI | A | B | C | D | E |
| Choo et al. 2012  | 12       | 25         | 13         | 34           | 20.7% | 1.28 [0.70, 2.37] | 7 | 7 | 7 | 7 | 7 |
| Kompan 2004       | 9        | 27         | 10         | 25           | 20.1% | 0.52 [0.25, 0.96] | 7 | 7 | 7 | 7 | 7 |
| Mahora 2004       | 21       | 100        | 30         | 100          | 25.2% | 0.70 [0.43, 1.14] | 7 | 7 | 7 | 7 | 7 |
| Moeen 2009        | 12       | 29         | 10         | 30           | 18.1% | 1.34 [0.84, 2.12] | 7 | 7 | 7 | 7 | 7 |
| Nigiwa 2013       | 3        | 14         | 6          | 14           | 8.0%  | 0.50 [0.13, 1.63] | 7 | 7 | 7 | 7 | 7 |
| Singh 1998        | 3        | 21         | 8          | 22           | 7.9%  | 0.39 [0.12, 1.28] | 7 | 7 | 7 | 7 | 7 |
| Total (95% CI)    | 216      | 225        | 100.0%     | 0.77 [0.53, 1.11] |       | 7 | 7 | 7 | 7 | 7 |

Total events: 60

Heterogeneity: I² = 6.88; Ch² = 8.13, df = 5 (P = 0.15); τ² = 38%

Test for overall effect: Z = 1.43 (P = 0.15)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Incomplete outcome data (attrition bias)
(D)Selective reporting (reporting bias)
(E) Other bias
## Bacteremia

| Study or Subgroup | Early EN Events | Early EN Total | Delayed EN Events | Delayed EN Total | Weight | Risk Ratio M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI | Risk of Bias A B C D E |
|-------------------|----------------|---------------|-------------------|------------------|--------|-------------------------------|-------------------------------|---------------------|
| Chiarello1990     | 3              | 10            | 7                 | 10               | 20.3%  | 0.43 [0.15, 1.20]             |                               | 7 7 7 7 7 7          |
| Cheardoko2012     | 4              | 23            | 3                 | 34               | 11.8%  | 1.81 [0.64, 5.19]             |                               | 7 7 7 7 7 7          |
| Eyre1993          | 2              | 19            | 0                 | 19               | 2.8%   | 5.00 [0.26, 97.70]            |                               | 7 7 7 7 7           |
| Malferla2004      | 20             | 100           | 30                | 100              | 60.1%  | 0.87 [0.41, 1.90]             |                               | 7 7 7 7 7 7         |
| Pupeiza2001       | 10             | 30            | 23                | 30               | 0.0%   | 0.43 [0.25, 0.72]             |                               | 7 7 7 7 7 7         |
| Singh1998         | 1              | 21            | 2                 | 22               | 4.3%   | 0.52 [0.05, 5.36]             |                               | 7 7 7 7 7           |
| **Total (95% CI)**| **175**        | **185**       | 100.0%            |                  |        | **0.72 [0.43, 1.19]**        |                               |                     |

**Total events**
- 30
- 42

**Heterogeneity**:
- Tau² = 0.05
- Chi² = 4.49, df = 4 (P = 0.34); I² = 11%

**Test for overall effect**: Z = 1.29 (P = 0.20)

### Risk of bias legend
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Incomplete outcome data (attrition bias)
- (D)Selective reporting (reporting bias)
- (E) Other bias

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![Graph showing SE(log[RR]) vs RR with study results marked and risk of bias assessment]
CRBSI

| Study or Subgroup | Early EN Events | Delayed EN Events | Total | Weight | Risk Ratio M-H, Random, 95% CI | Risk of Bias |
|-------------------|-----------------|-------------------|-------|--------|--------------------------------|--------------|
| Iyer1993          | 1               | 19                | 1     | 1      | 1.00 [0.07, 14.83]             | A             |
| Moses2009         | 3               | 29                | 4     | 30     | 0.78 [0.19, 3.17]              | B             |
| Total events      | 4               | 49                | 5     | 48     | 0.82 [0.24, 2.83]              | C             |

Heterogeneity: Tau² = 0.00; CH² = 0.03, df = 1 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.76)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Incomplete outcome data (attrition bias)
(D) Selective reporting (reporting bias)
(E) Other bias
Added hand searched paper: n=4

Titles initially screened: n=694

1st. Screening (abstracts): 196 articles

exclusion: 150

Excluded by full text screening: 33 articles
Reasons of exclusion (dupulicated)
Wrong outcome: 4
Duplicate: 2
Wrong population: 19
Wrong study design: 13
Wrong drug: 7
Language: 4
Background article: 1
Wrong publication type: 1

2nd Screening (full text): 46 articles

Included articles: 13
| Study                        | Allocation concealment (selection bias) | Random sequence generation (selection bias) | Allocation concealment of participants and personnel (performance bias) | Allocation concealment of outcome assessment (detection bias) | Detection of outcome assessment (detection bias) | Reporting (attrition bias) | Reporting (other bias) |
|-----------------------------|----------------------------------------|--------------------------------------------|--------------------------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------------|--------------------------|------------------------|
| Chazelle1990                |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Chowdrika2012               |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Elter1993                   |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Kompan1999                  |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Kompan2004                  |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Malhotra2004                |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Moses2005                   |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Nguyen2012                  |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Peck2004                    |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Petrov2013                  |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Pupeza2003                  |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Strong2006                  |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |
| Sun2013                     |                                         | 1                                          | 1                                                                        | 1                                                              | 1                                             | 1                        | 1                      |