實證醫學 病例討論報告

Evidence-Based Medicine

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報告日期：101.5.15

腎臟內科

Outline

- Clinical scenario-臨床場景
- Asking-提出問題
- Acquire- 搜尋資料
- Appraisal-嚴格評讀
- Apply-臨床應用
- Audit-自我評估

Clinical scenario

PATIENT'S PROFILE

- This 68 y/o man has history of
  - DM noted for 15+ yr
  - Hypertension

This time,

- Suffered from fever, poor appetite and diarrhea for 2 weeks
- Admitted to nephrology ward due to sepsis
- Lab: BUN: 60.5; Creatinine: 2.05; CRP: 67; no pyuria
- CXR: pulmonary congestion, cardiomegaly
- Physical exam: RUQ pain when palpation but no muscle guarding

- Impression :
  - Sepsis, suspect intraabdominal infection

AFTER ADMISSION...

We would like to arrange abdominal CT to survey infection focus.

=> however, poor renal function was noted

=> Medication to prevent chronic kidney disease with acute deterioration

Risk factors

Patient Related

Chronic kidney disease[3,13-19]

Diabetes mellitus[13,16,17,19]

Urgent/elective procedure[16]

Intra-aortic balloon pump[16,17,20]

Congestive heart failure[13,15,17,20]

Age[3,17]

Hypertension[21,22]

Low hematocrit[17,23]

Hypotension[17,22]

Left ventricular ejection fraction <40%[22]

Not Patient Related

Contrast properties

- High osmolar contrast[7,24]
- Ionic contrast[25-28]
- Contrast viscosity[29,30]

Contrast volume[3,13,16-19,31-34]

JAMA. 2006;295:2765-2779

ASKING

Background question

Q1: What is contrast-induced nephropathy?
Q2: How many types of radiocontrast agents?
Q3: What is the pathogenesis of contrast-induced nephropathy?

Q1 What is contrast-induced nephropathy?

- 資料出處：Uptodate

  Prevention of contrast-induced nephropathy

- The administration of radiocontrast media can lead to a usually reversible form of acute kidney injury
  - Begins soon after the contrast is administered.
  - In most cases, there are no permanent sequelae

Q2: How many types of radiocontrast agents?

- 資料出處：Uptodate

  Prevention of contrast-induced nephropathy

- First generation agents
  - ionic monomers; they are highly hyperosmolal (approximately 1400 to 1800 mosmol/kg) compared with the osmolality of plasma.
- Second generation agents, such as iohexol
  - nonionic monomers with a lower osmolality than the first generation radiocontrast media; however, they still have an increased osmolality (500 to 850 mosmol/kg) compared with plasma
  - The newest nonionic contrast agents are iso-osmolal, being dimers with an osmolality of approximately 290 mosmol/kg (iodixanol is the first such agent)

Q3 What is the pathogenesis of contrast-induced nephropathy ?

- 資料出處：Uptodate

  Pathogenesis, clinical features, and diagnosis of contrast-induced nephropathy

- Some studies show evidence of acute tubular necrosis (ATN), although the mechanism is not well understood
  - The two major theories are
    - Renal vasoconstriction resulting in medullary hypoxemia, possibly mediated by alterations in nitric oxide, endothelin and/or adenosine
    - Direct cytotoxic effects of the contrast agents

- If ATN does occur, it is not clear why recovery occurs within a few days in contrast nephropathy, compared to one to three weeks with ATN due to other causes
- There are at least two possibilities to explain these findings:
  - The degree of tubular necrosis is much less severe than seen in other settings.
  - There is postischemic or posttoxic tubular dysfunction in which the tubular cells remain morphologically normal

將搜尋的結果應用到我的病人

- Chest CT with contrast中使用的radiocontrast agents有可能會造成contrast-induced nephropathy
- 若選擇Second generation agents的nonionic monomers，由於lower osmolality，較不易造成contrast-induced nephropathy

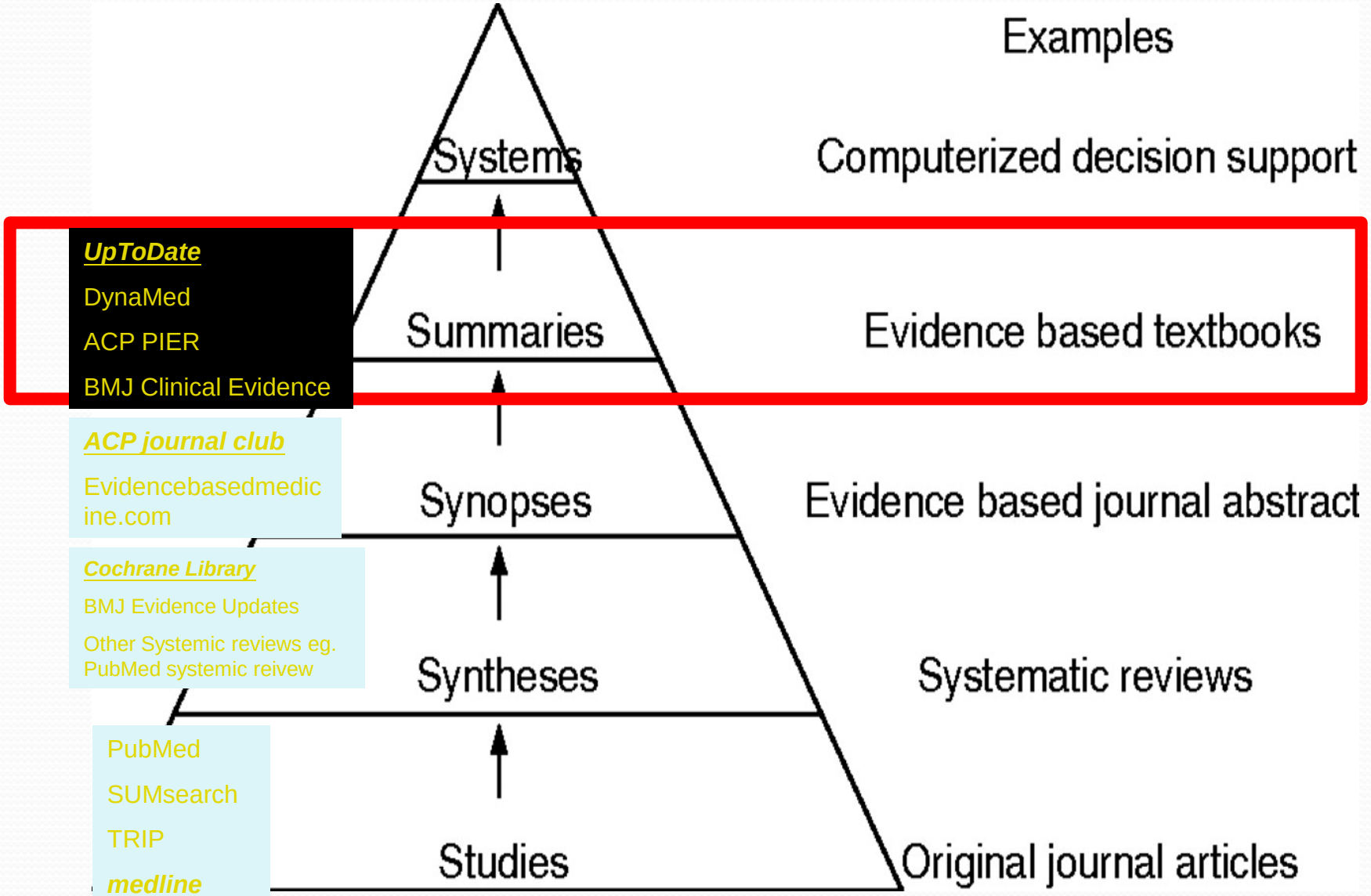
Foreground questions

Does theophylline benefit to the patients who would accept contrast enhancement about lowering morbidity of contrast-induced nephropathy?

PICOT

Patient	Patients with impaired renal function who would accept contrast enhancement -CT
Intervention	With theophylline
Comparison	Without theophylline
Outcome	Renal function progression (Morbidity of contrast-induced nephropathy)
Time	Not confined

Search strategy: 5S model



搜尋 UpToDate

- Key words
  - theophylline
  - Contrast-induced nephropathy

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Click related term for theophylline: methylxanthines

Topic Outline

- **All Topics**
- **Adult**
- **Pediatric**
- **Patient**
- **Graphics**

- Prevention of contrast-induced nephropathy
- Pathogenesis, clinical features, and diagnosis of contrast-induced nephropathy
- Complications of endovascular abdominal aortic repair
- Theophylline use in asthma
- Theophylline: Drug information
- Theophylline: Pediatric drug information
- Role of methylxanthines in the treatment of COPD
- Theophylline: Patient drug information
- Theophylline poisoning
- Ephedrine and theophylline: International drug information
- Management of apnea of prematurity
- Complications of diagnostic cardiac catheterization
- Pharmacologic treatment of obstructive sleep apnea in adults
- Chronic asthma in children younger than 12 years: Controller medications
- Arrhythmias in COPD
- Management of the patient with severe COPD and coronary artery disease
- Erythrocytosis following renal transplantation
- Idiopathic systemic capillary leak syndrome
- Treatment of sleep-disordered breathing in COPD
- Drugs that should be avoided or used with caution in patients with heart failure
- Cheyne-Stokes breathing and obstructive sleep apnea in heart failure
- Disorders of ventilatory control

Prevention of contrast-induced nephropathy

- Inhibition of renal vasoconstriction
  - theophylline or aminophylline (presumably via inhibition of the effect of adenosine), nifedipine, captopril, prostaglandin E or I2, low-dose dopamine, or fenoldopam

- A 2005 meta-analysis of nine controlled trials of 585 patients

→administered theophylline (versus controls)

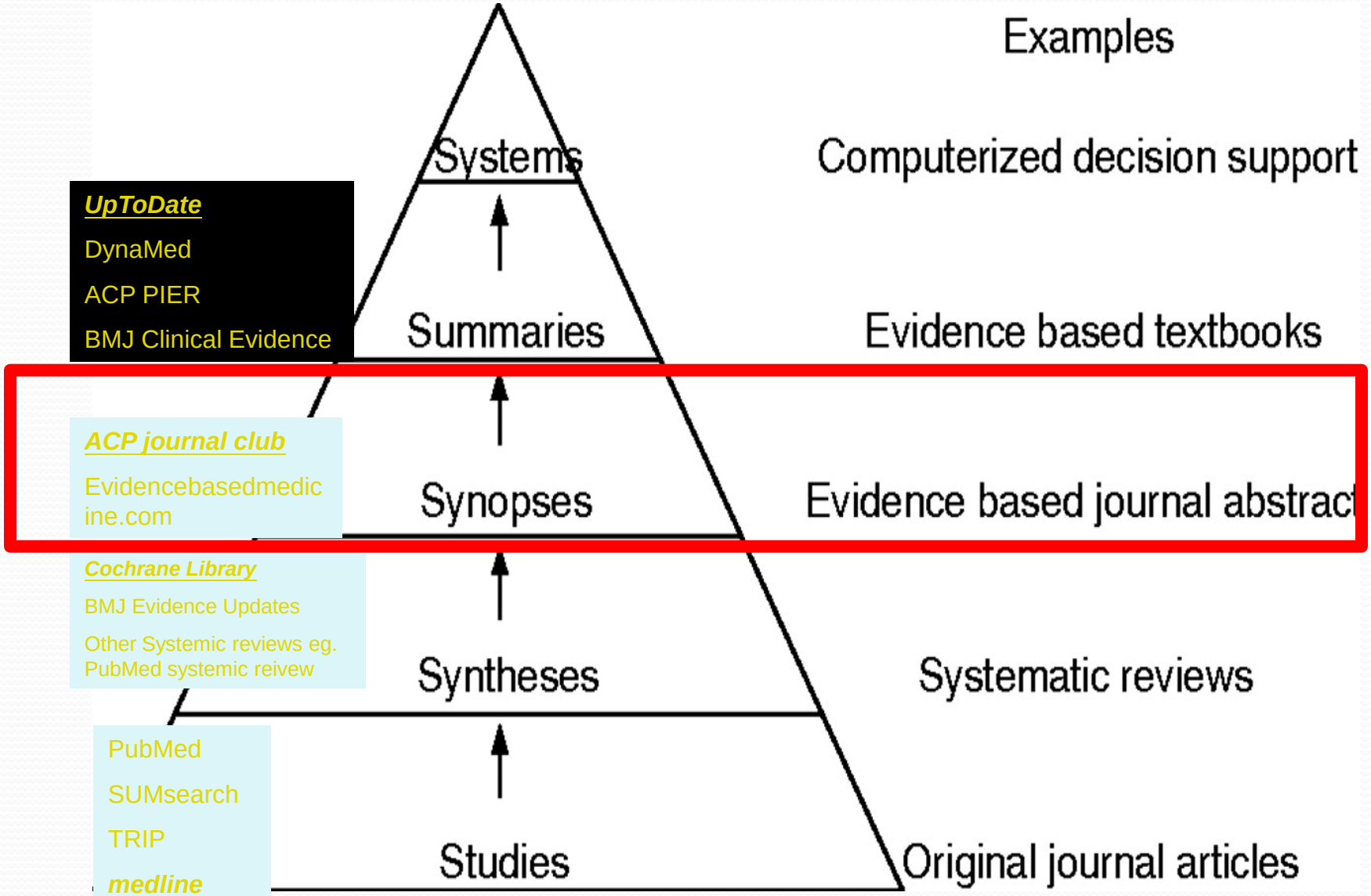
→found that theophylline may provide some benefit, although,

  - the absolute benefit was small
  - relatively low risk (only one case required dialysis)

將systemic搜尋的結果應用到我的病人

- Theophylline是adenosine antagolist，有助於降低renal vasoconstriction，有達到預防cotrast induced nephropathy的理論基礎

Search strategy: 5S model



搜尋 ACP Journal club

- Key words
  - theophylline
  - Contrast-induced nephropathy

SYNOPSES SEARCH RESULTS

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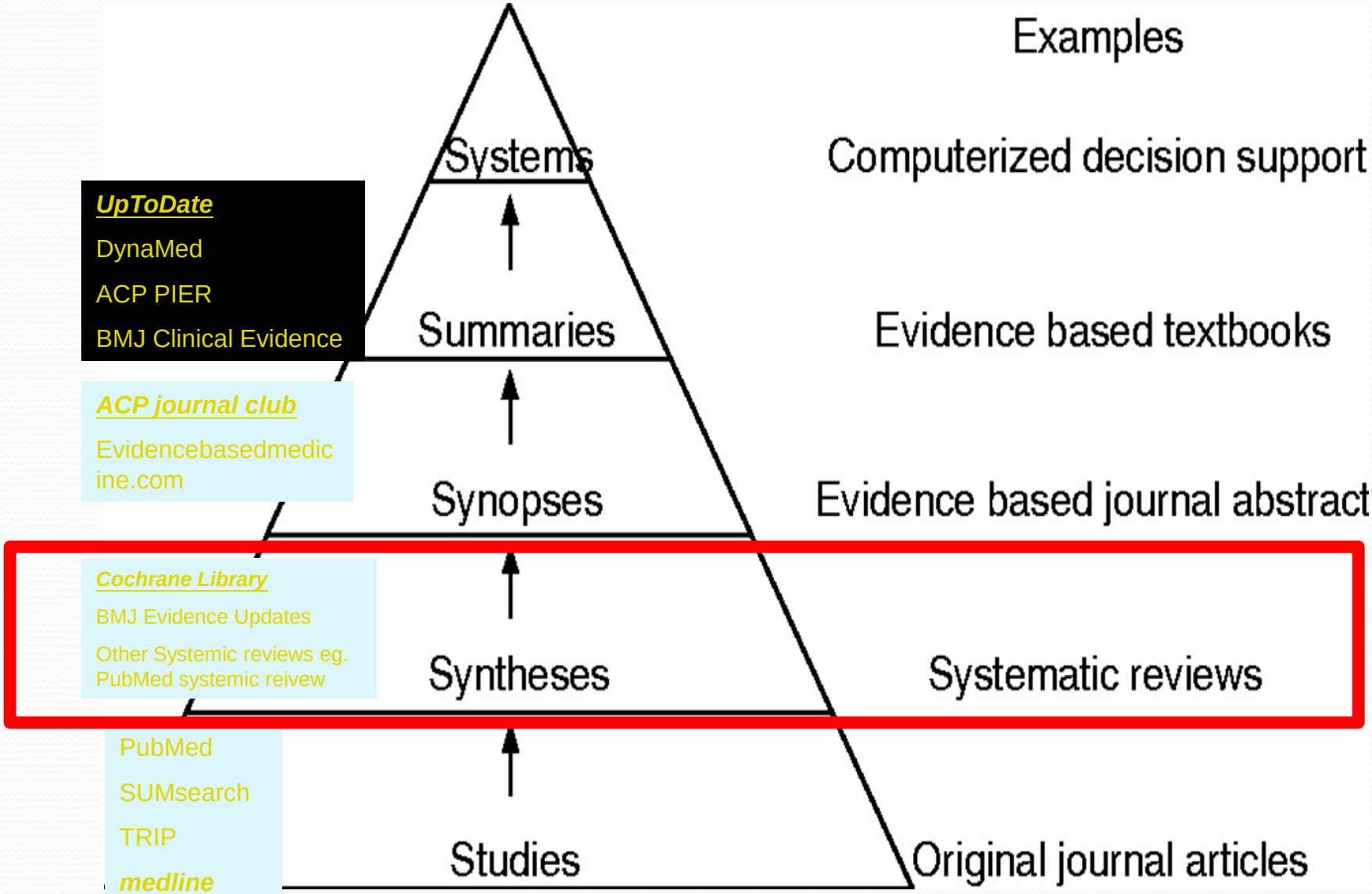
2011 - The RenalGuard system reduced kidney injury more ...

將**SYNOPSES**的搜尋結果應用到我病人身上

- 並無探討到使用theophylline應用在Contrast-induced nephropathy 的相關文章

Search strategy: 5S model



搜尋 Cochrane library

- Key words
  - theophylline
  - Contrast-induecd nephropathy

SYNTHESIS SEARCH RESULTS

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THE COCHRANE LIBRARY
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There are **1** results out of **17084 records** for: "**theophylline contrast nephropathy** in **Title, Abstract or Keywords** in **Database of Abstracts of Reviews of Effects**"

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Record Information — Sort by: Record Title | **Match %** | Date

Theophylline for prevention of contrast-induced nephropathy: a systematic review and meta-analysis (Structured abstract)
Centre for Reviews and Dissemination
Original Author(s): S M Bagshaw, W A Ghali
2005

Select All (to export citations)

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View: **1**

Theophylline for prevention of contrast-induced nephropathy: a systematic review and meta-analysis (Structured abstract)

- Bagshaw S M, Ghali W A. Theophylline for prevention of contrast-induced nephropathy: a systematic review and meta-analysis. *Archives of Internal Medicine*.2005;**165**(10):1087-1093..

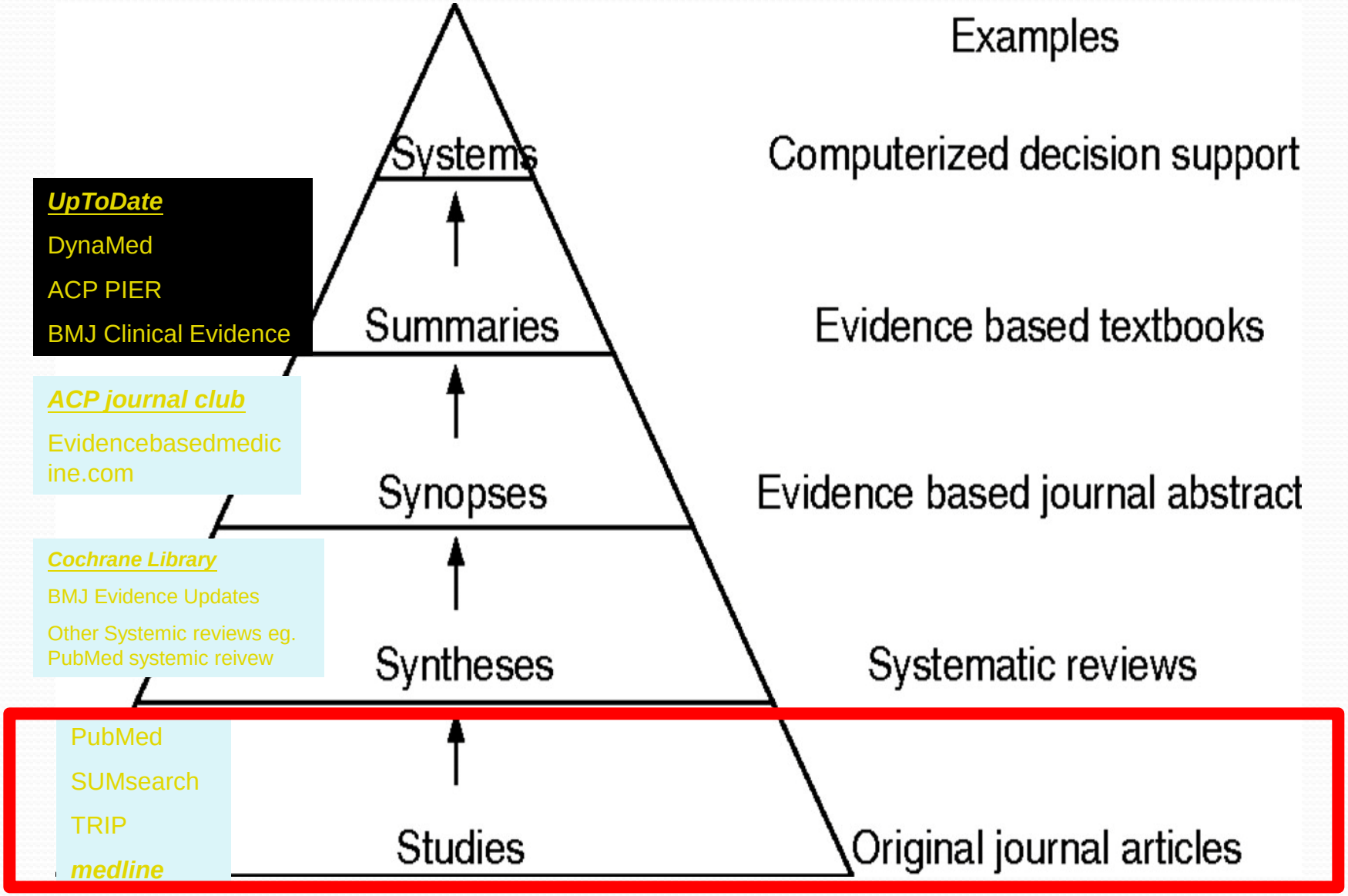
- ***Authors' objectives***
  To assess the efficacy of theophylline, an adenosine antagonist, for the prevention of contrast -induced nephropathy (CIN)
- ***Study selection: study designs***
  - randomized controlled trials
- ***Study selection: outcomes***
  - incidences of CIN

- ***Results of the review***
  - Nine RCTs involving 585 participants were included in the review.
  - no statistically significant reduction in the incidence of CIN with the use of theophylline (OR 0.40, 95% CI: 0.14, 1.16, P=0.09)
  - CIN requiring dialysis was uncommon and was reported in only 1 case.
  - no evidence of publication bias
- ***conclusions***
  - The evidence on the use of theophylline for the prevention of CIN is suggestive of possible benefit but remains inconclusive.

將**SYNTHESIS**的搜尋結果應用到我病人身上

- 此篇review在統計上並無法降低contrast induced nephropathy的incidence rate，還是需要有更大型的trial來討論是否該例行性使用theophylline和其使用上的 risk

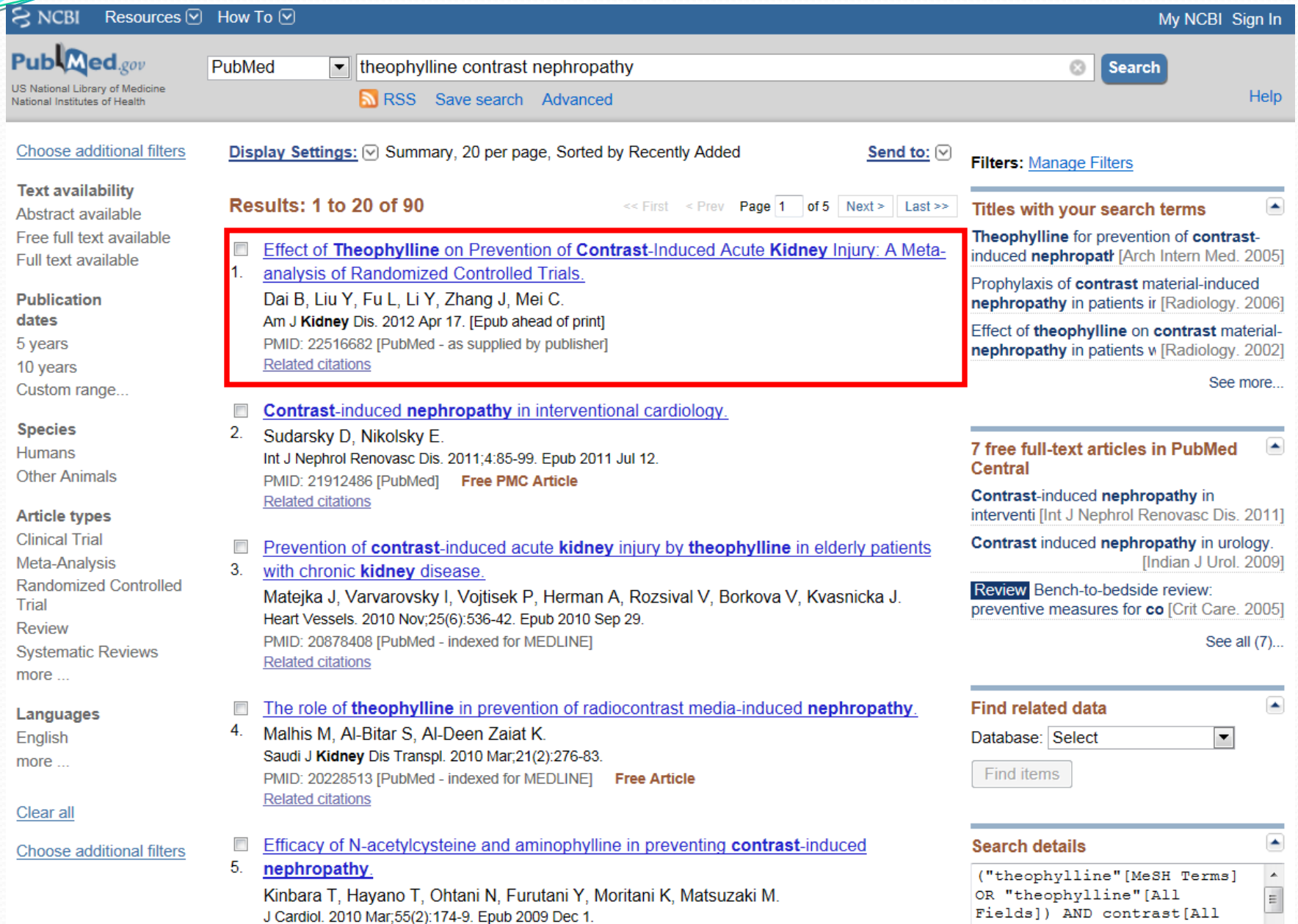
Search strategy: 5S model



搜尋 PubMed~

- Key words
  - theophylline
  - Contrast nephropathy

STUDY SEARCH RESULTS



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1. Effect of **Theophylline** on Prevention of **Contrast**-Induced Acute **Kidney** Injury: A Meta-analysis of Randomized Controlled Trials.
   Dai B, Liu Y, Fu L, Li Y, Zhang J, Mei C.
   Am J **Kidney** Dis. 2012 Apr 17. [Epub ahead of print]
   PMID: 22516682 [PubMed - as supplied by publisher]
   Related citations

2. **Contrast**-induced **nephropathy** in interventional cardiology.
   Sudarsky D, Nikolsky E.
   Int J Nephrol Renovasc Dis. 2011;4:85-99. Epub 2011 Jul 12.
   PMID: 21912486 [PubMed] **Free PMC Article**
   Related citations

3. Prevention of **contrast**-induced acute **kidney** injury by **theophylline** in elderly patients with chronic **kidney** disease.
   Matejka J, Varvarovsky I, Vojtisek P, Herman A, Rozsival V, Borkova V, Kvasnicka J.
   Heart Vessels. 2010 Nov;25(6):536-42. Epub 2010 Sep 29.
   PMID: 20878408 [PubMed - indexed for MEDLINE]
   Related citations

4. The role of **theophylline** in prevention of radiocontrast media-induced **nephropathy**.
   Malhis M, Al-Bitar S, Al-Deen Zaiat K.
   Saudi J **Kidney** Dis Transpl. 2010 Mar;21(2):276-83.
   PMID: 20228513 [PubMed - indexed for MEDLINE] **Free Article**
   Related citations

5. Efficacy of N-acetylcysteine and aminophylline in preventing **contrast**-induced **nephropathy**.
   Kinbara T, Hayano T, Ohtani N, Furutani Y, Moritani K, Matsuzaki M.
   J Cardiol. 2010 Mar;55(2):174-9. Epub 2009 Dec 1.

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Theophylline for prevention of **contrast**-induced **nephropath** [Arch Intern Med. 2005]

Prophylaxis of **contrast** material-induced **nephropathy** in patients ir [Radiology. 2006]

Effect of **theophylline** on **contrast** material-**nephropathy** in patients w [Radiology. 2002]

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Contrast-induced **nephropathy** in interventi [Int J Nephrol Renovasc Dis. 2011]

Contrast induced **nephropathy** in urology. [Indian J Urol. 2009]

Review Bench-to-bedside review: preventive measures for **co** [Crit Care. 2005]

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("theophylline"[MeSH Terms] OR "theophylline"[All Fields]) AND contrast[All

- ***Title***

  Effect of Theophylline on Prevention of Contrast-Induced Acute Kidney Injury: A Meta-analysis of Randomized Controlled Trials

- ***Author***
  - *Bing Dai, MD,1* Yawei Liu, MD,1* Lili Fu, MS,1 Yongchuan Li, MD,1 Jiayou Zhang, MD,2and Changlin Mei, MD1*
- ***Background***
  - *Whether treatment with adenosine receptor antagonists such as theophylline can prevent contrast-induced acute kidney injury (AKI) remains controversial.*
- ***Study Design***
  - *We conducted a meta-analysis of randomized controlled trials using MEDLINE (1966 to July 2011), EMBASE (1980 to July 2011), Web of Science (1986 to July 2011), and the Cochrane Central Register of Controlled Trials (1996 to July 2011), without language restriction.*

- ***Setting & Population:***
  - *Patients undergoing contrast procedures*
- ***Selection Criteria for Studies:***
  - *Randomized controlled trials assessing adenosine antagonists versus control for prevention of contrast-induced AKI.*
- ***Intervention:***
  - *Adenosine antagonists : theophylline or aminophylline*
- ***Outcomes:***
  - *Contrast-induced AKI, change in serum creatinine level, requirement of dialysis, and in-hospital mortality.*

- AKI: defined as an increase in baseline SCr level of
- 25% or an absolute increase of 0.5 mg/dL

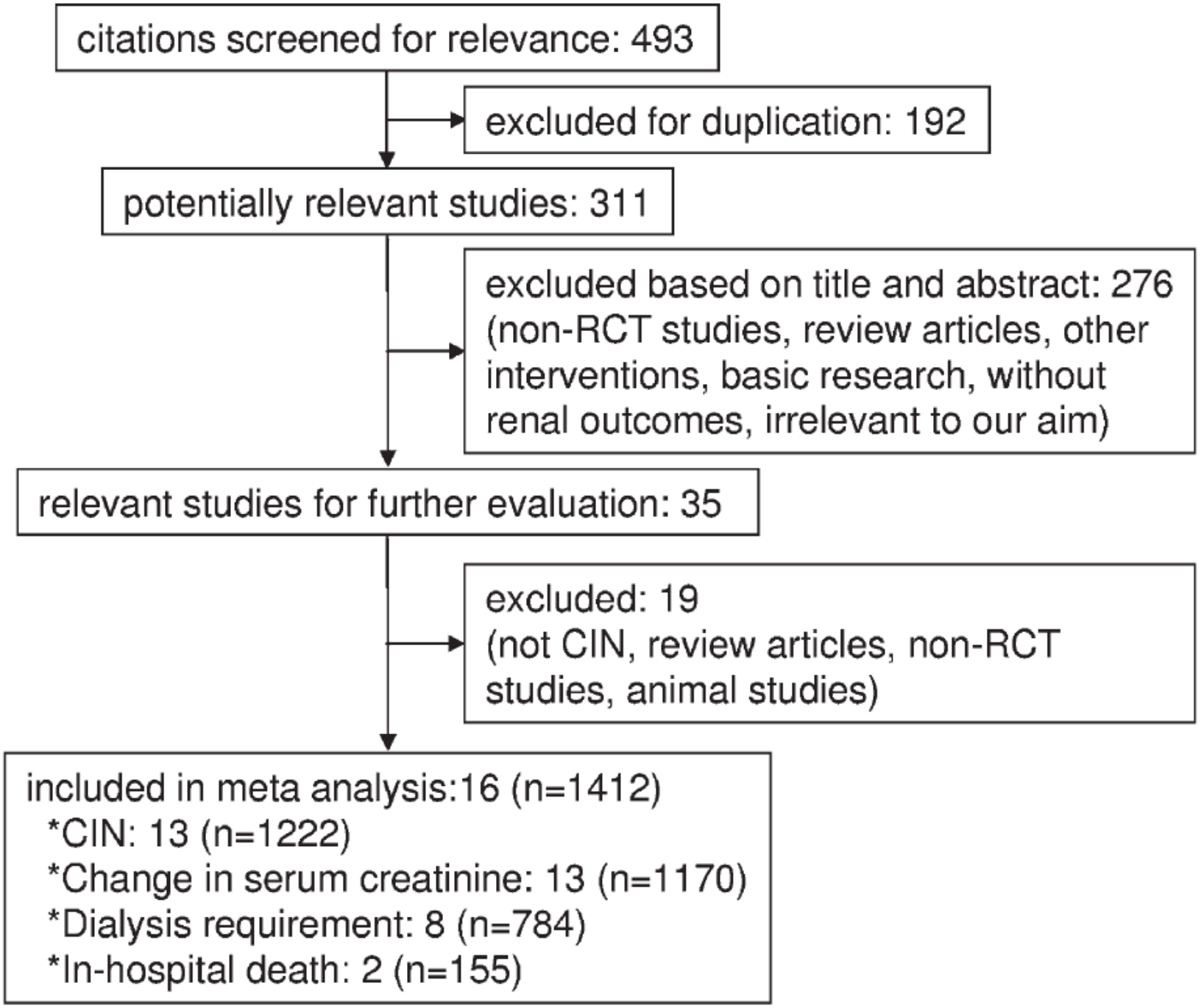
citations screened for relevance: 493
excluded for duplication: 192
potentially relevant studies: 311
excluded based on title and abstract: 276 (non-RCT studies, review articles, other interventions, basic research, without renal outcomes, irrelevant to our aim)
relevant studies for further evaluation: 35
excluded: 19 (not CIN, review articles, non-RCT studies, animal studies)
included in meta analysis:16 (n=1412)
*CIN: 13 (n=1222)
*Change in serum creatinine: 13 (n=1170)
*Dialysis requirement: 8 (n=784)
*In-hospital death: 2 (n=155)

Table S1. Quality of included RCTs

Author, Year	Jadad Quality Score†	Type of Blinding	Method of Double Blinding Described and Appropriate	Randomization Process Described and Adequate	Adequate Concealed Allocation	Description of Withdrawals And Dropouts	Intention-to-Treat Analysis Performed	Important Baseline Differences Present	Inclusion and Exclusion Criteria Specified
Grandhi 1992	1	NS	NS	NO	NS	NS	NS	NS	NS
Erley 1994	3	double	NO	NO	NS	YES	NO	NO	YES
Katholi 1995	1	NS	NS	NO	NS	NS	YES	NO	YES
Kolonko 1998	2	double	NS	NO	NS	NS	YES	NO	YES
Abizaid 1999	3	NO	NO	YES	NO	YES	YES	YES higher baseline Scr lever in control group	YES
Erley 1999	3	double	NO	NO	NS	YES	NO	NO	YES
Huber 2002	2	double	NO	NO	NS	NS	YES	NO	YES
Kapoor 2002	1	NS	NS	NO	NS	NS	NS	NO	YES
Huber 2003	1	NS	NS	NO	NS	NS	YES	NO	YES
Dussol 2006	3	NO	NO	YES	NS	YES	NO	NO	YES
Huber 2006	1	NS	NS	NO	NS	NS	NS	YES higher baseline value for BUN levels in NAC + theophylline group	YES
Baskurt 2009	2	NS	NS	NO	NS	YES	YES	YES higher mean contrast volume in the NAC + theophylline group	YES
Matejka 2010	4	double	YES	NO	YES	YES	NO	NO	YES
Kinbara 2010	1	NS	NS	NO	NS	NS	YES	NO	YES
Malhis 2010	1	NS	NS	NO	NS	NS	YES	YES higher baseline value for Scr levels in theophylline group	YES
Rohani 2010	2	double	NO	NO	NS	NS	YES	NO	YES

Abbreviation: NS, not specified or available.

Table 1. Summary of Study and Patient Characteristics Included in the Meta-analysis

Study, Year	No. of Patients	DM (%)	Procedure and Contrast Type	Contrast Media Volume (mL)		Baseline SCr (μmol/L [mg/dL])		Theo or Amino Protocol	Hydration Procedure	Primary Outcome
				Theo	Ctrl	Theo	Ctrl			
Gandhi et al,[17] 1992	21	NR	NR; iopromide or ioxaglate	NR	NR	NR	NR	Theo 125 mg orally 2×/d 24 h before & 48 h after	NR	NR
Erley et al,[18] 1994	39	15	CT or AG; iopamidol	>100	>100	1.2 [0.5]	1.2 [0.9]	Theo 5 mg/kg IV 45 min before	NR	ΔGFR[a] at 48 h
Katholi et al,[19] 1995	93	18	CAG or LVG; iopamidol or sodium diatrizoate	111	110	1.25	1.25	Theo 2.88 mg/kg orally every 12 h 1 h before & 48 h after	1.43 mL/kg/h 1 h before & 72 h after or dextrose[b] 3 d	ΔCCr at 48 h
Kolonko et al,[20] 1998	58	0	X-ray; uropolinum	40	40	1.01	1.28	Theo 165 mg IV 30 min prior	No hydration	ΔSCr at 24 h
Abizaid et al,[21] 1999	40	55	CAG; ioxaglate	198	182	1.9 [0.4]	2.3 [0.8]	Amino 4-mg/kg bolus then 0.4 mg/kg/h IV 2 h before	0.45% saline solution 1 mL/kg/h 12 h before & 12 h after	↑ SCr ≥25% at 48 h
Erley et al,[22] 1999	64	30	CT or DSA; iopromide	130	120	1.9 [0.5]	1.7 [0.4]	Theo 270 mg orally every morning & 540 mg orally every night 2 d before & 3 d after	2-2.5 L fluid (orally or 0.45% saline solution IV) 24 h before & 24 h after	↑ SCr ≥0.5 mg/dL within 72 h
Huber et al,[23] 2002	100	34	CAG, CT, other; iomeprol	197	217	2.07 [0.94]	1.92 [0.76]	Theo 200 mg IV 30 min before	≥2 L/d advised	↑ SCr >0.5 mg/dL within 48 h
Kapoor et al,[24] 2002	70	100	CAG; diatrizoate meglumine	78	80	1.16 [0.18]	1.19 [0.23]	Theo 200 mg orally 2×/d 24 h before & 48 h after	0.9% saline solution 1 mL/kg/h 12 h before & 12 h after	↑ SCr ≥25% or ↓ GFR ≥25% within 48 h
Huber et al,[25] 2003	100	31	CAG; iomeprol 350	197	217	1.65 [0.41]	1.72 [0.69]	Theo 200 mg IV 30 min before	≥2 L/d advised	↑ SCr >0.5 mg/dL within 48 h
Dussol et al,[26] 2006	157	28	CAG, CT, other; iopromide, iobitridol, ioxaglate	133	115	2.42 [1.5]	2.35 [0.95]	Theo 5 mg/kg orally in 1 dose 1 h before	0.9% saline solution 15 mL/kg 6 h before	↑ SCr >0.5 mg/dL within 48 h

Table 1 (Cont'd). Summary of Study and Patient Characteristics Included in the Meta-analysis

Study, Year	No. of Patients	DM (%)	Procedure and Contrast Type	Contrast Media Volume (mL)		Baseline SCr (μmol/L [mg/dL])		Theo or Amino Protocol	Hydration Procedure	Primary Outcome
				Theo	Ctrl	Theo	Ctrl			
Huber et al,[27] 2006	99	26	CAG, CT, other; iomeprol	157	151	1.28 [0.74]	1.25 [0.74]	Theo 200 mg IV 30 min before + NAC	No specific hydration protocol	↑ SCr >0.5 mg/dL within 48 h
Baskurt et al,[28] 2009	145	30	CAG; ioversol	131	116	1.47 [0.27]	1.39 [0.24]	Theo 200 mg orally 2×/d before & on the day + NAC	0.9% saline solution 1 mL/kg/h 12 h before & 12 h after	↑ SCr >0.5 mg/dL within 48 h
Matejka et al,[29] 2010	56	75	CAG and/or PCI; iodixanol	95	94	2.02 [0.45]	2.06 [0.59]	Theo 205.7 mg IV 1 h before	0.9% saline solution 0.5 mL/kg/d 3 d after	ΔSCr within 48 h
Kinbara et al,[30] 2010	30	40	CAG and/or PCI; iopamidol	142	141	0.97 [0.29]	0.94 [0.21]	Amino 250 mg IV 30 min before	0.9% saline solution 1 mL/kg/h 30 min before & 10 h after	↑ SCr >0.5 mg/dL within 48 h
Malhis et al,[31] 2010	280	32.5	CAG, PCI, CT, other; iohexol, iopamidol, iodixanol	137	144	1.38 [0.79]	1.21 [0.48]	Theo 200 mg orally 2×/d 24 h before & 48 h after; or 200 mg IV 30 min before & 200 mg orally 2×/d 48 h after	1-2 L sodium bicarbonate (150 mEq/L) 12 h after	For baseline SCr <2 mg/dL, ↑ SCr ≥0.5 mg/dL at 48 h; for baseline SCr ≥2 mg/dL, ↑ SCr >25% at 48 h
Rohani,[32] 2010	60	18	CAG; iohexol	200	210	1.93 [0.21]	1.84 [0.54]	Amino 250 mg IV 30 min before	0.9% saline solution 1.0-1.5 mL/kg/h 3-12 h before & 6-24 h after	↑ SCr >0.5 mg/dL within 48 h

- ***Results:***
  - *16 trials (1,412 participants) were included.*
  - *Theophylline significantly decreased the risk of contrast-induced AKI (13 trials, 1,222 patients; risk ratio, 0.48; 95% CI, 0.26-0.89; P= 0.02; I2= 45%)*
  - *protective effect on the absolute change in serum creatinine concentration (13 trials, 1,170 patients; standardized mean difference, 0.31 mg/dL; 95% CI, 0.50 to 0.11; P= 0.002; I2= 60%)*
  - *Meta-regression showed a significant relation between the relative risk of contrast nephropathy and baseline serum creatinine level or Jadad score.*
  - *No clear effects of treatment on risk of dialysis and in-hospital mortality were identified*
- ***Conclusions:***
  - *Theophylline treatment significantly reduced the incidence of contrast-induced AKI and had a modest improvement on kidney function after contrast exposure in the general population.*
  - *However, beneficial effects of theophylline were not observed in patients with high baseline creatinine values (serum creatinine 1.5 mg/dL).*
  - *In addition, the long-term effect of this agent on more clinically important outcomes was not established.*
  - *Future large-scale high-quality multicenter trials in participants with different underlying risks of contrast-induced AKI and that incorporate the evaluation of clinically relevant outcomes are required.*

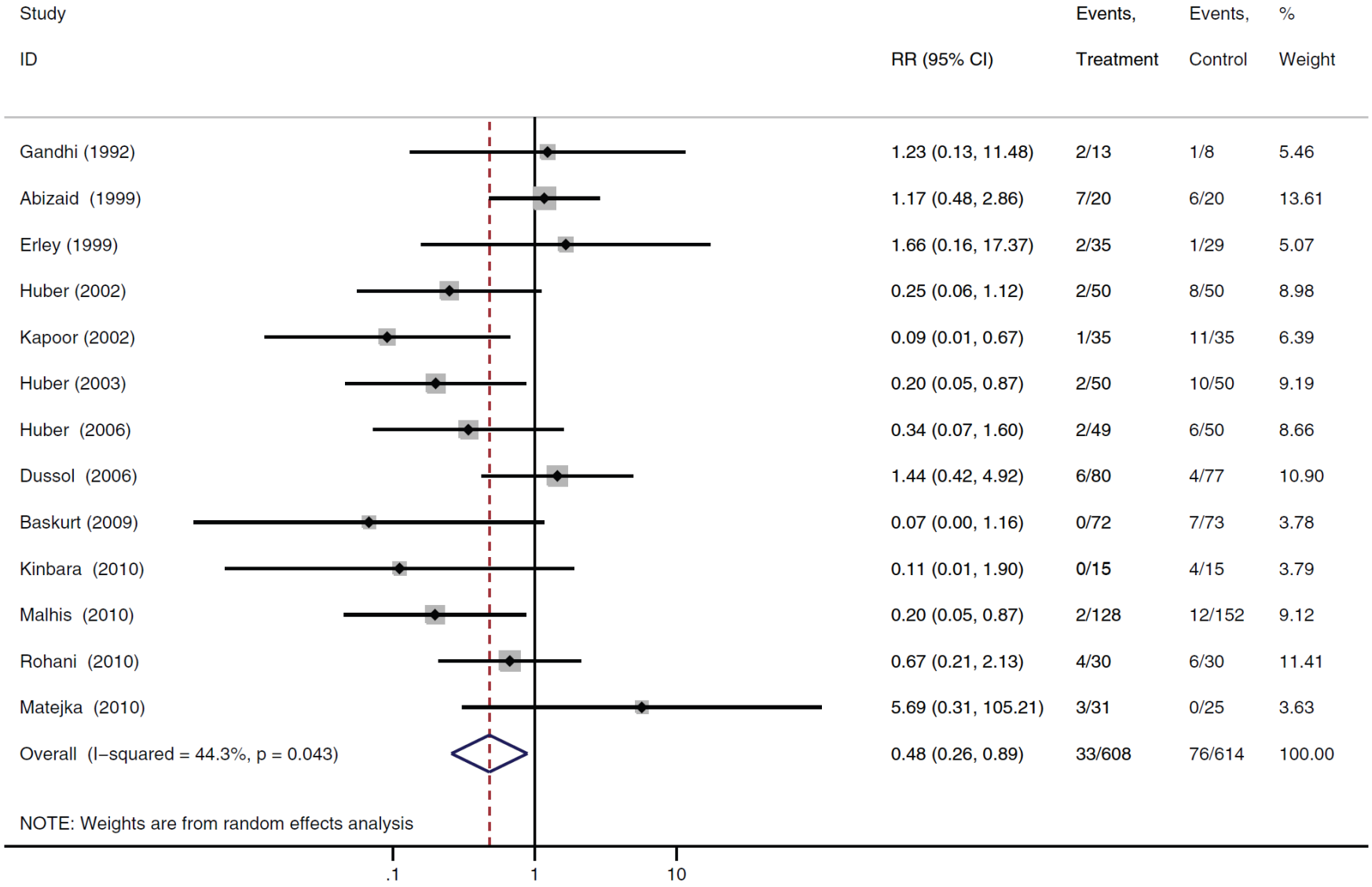

Figure 2. Forest plot of risk ratios (RRs) and 95% confidence intervals (CIs) for the incidence of contrast-induced acute kidney injury in patients assigned to theophylline therapy versus control.

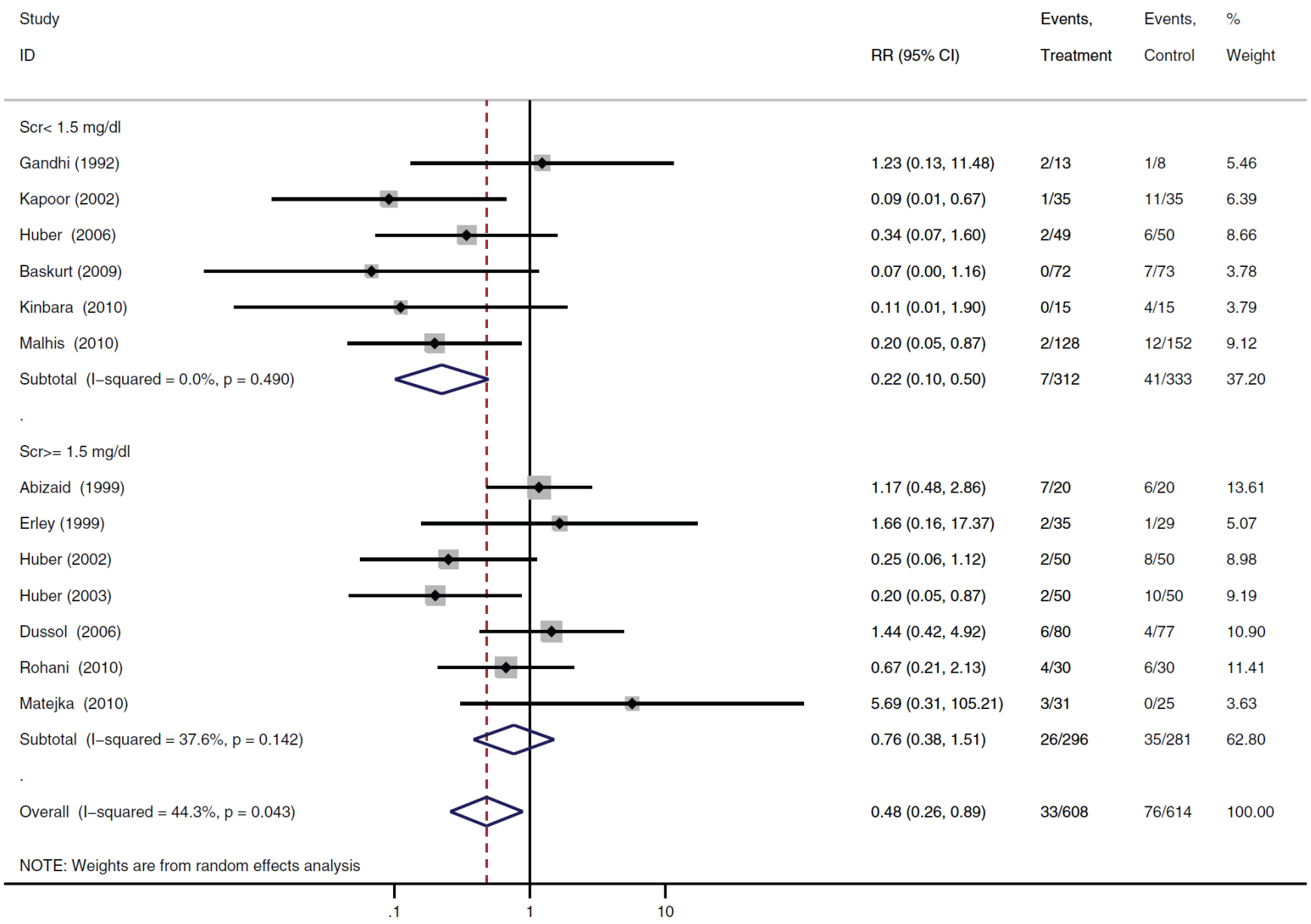

Figure 3. Forest plot of risk ratios (RRs) and 95% confidence intervals (CIs) for the incidence of contrast-induced acute kidney injury in patients assigned to theophylline therapy versus control according to renal function. Abbreviation: Scr, serum creatinine.

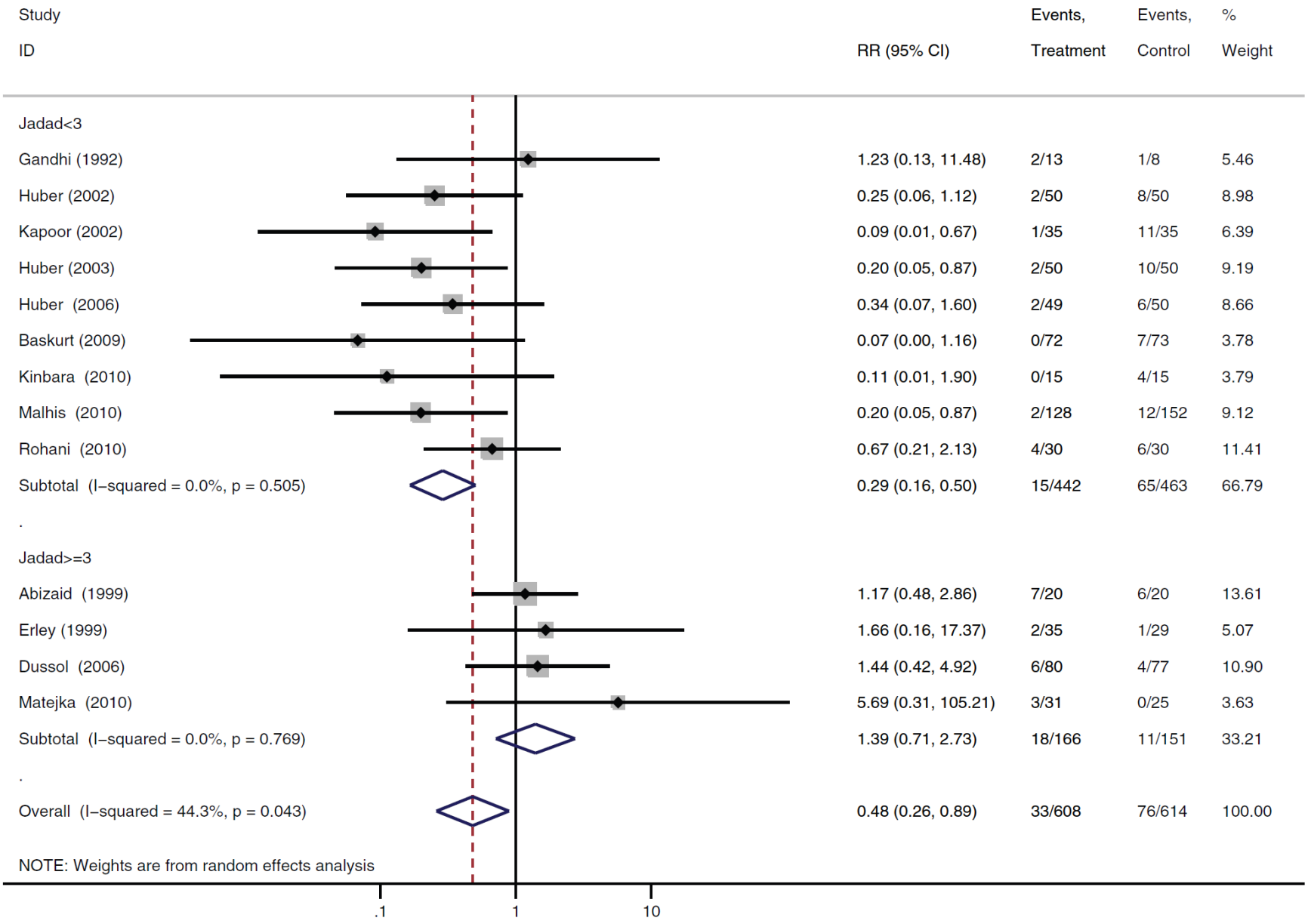

Figure 4. Forest plot of risk ratios (RRs) and 95% confidence intervals (CIs) for the incidence of contrast-induced acute kidney injury in patients assigned to theophylline therapy versus control according to Jadad score.

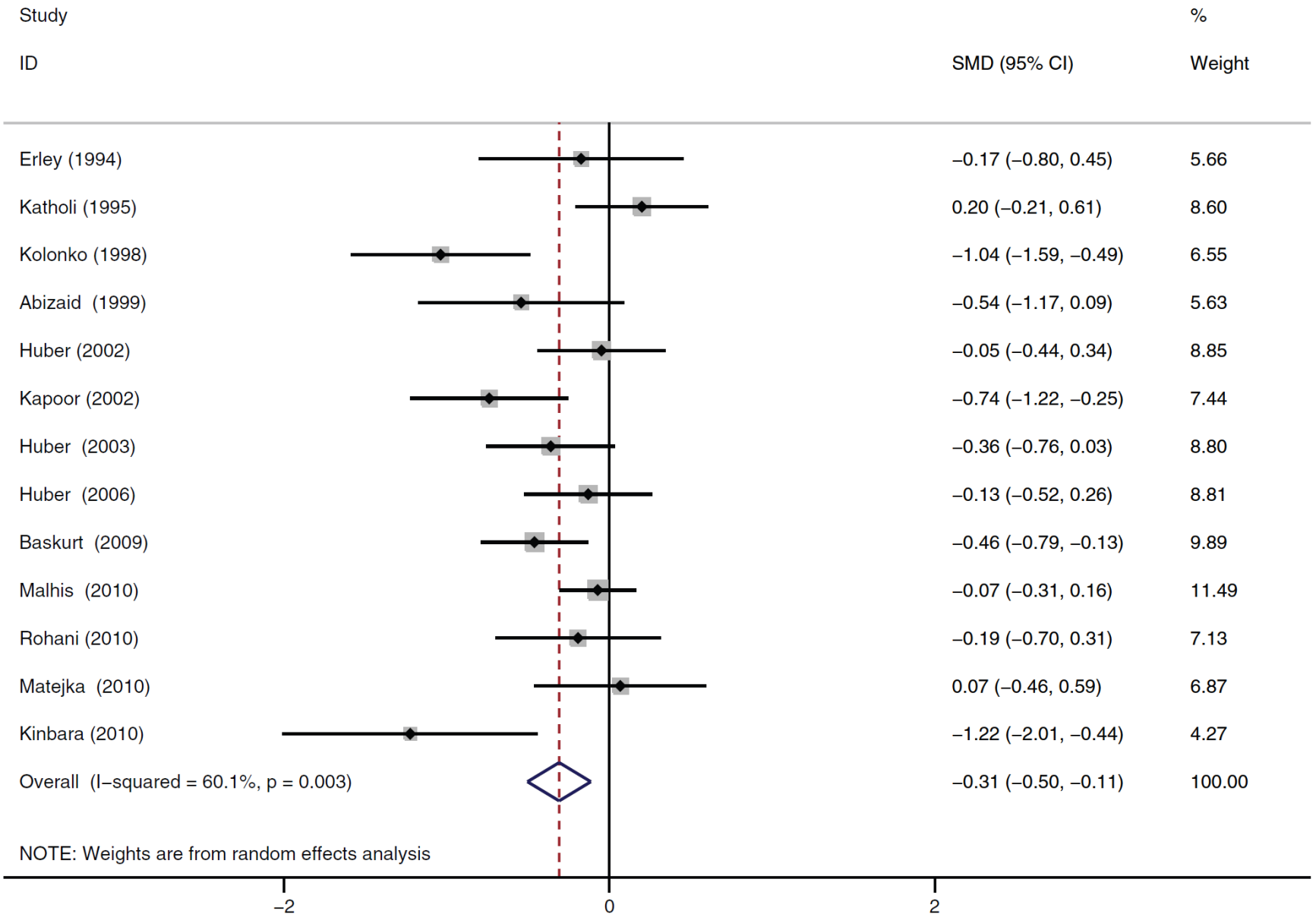

Figure 5. Forest plot of differences in serum creatinine levels between the theophylline and control groups at 48 hours after contrast media administration from 13 trials. Error bars represent 95% confidence intervals (CIs). Abbreviation: SMD, standardized mean difference.

Critical Appraisal

Valid: systemic review worksheet

Importance: what were the result?

Applicability: population and feasibility

證據等級

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

Appraisal

Step 1：AAMPICOT將文獻分析

What question did the systematic review addressed (PICO) 想要回答什麼問題？

■是	□ 否	□ 不清楚

評論：

- **The patient accept contrast therapy or image [P]**
- **Theopylline use [I]**
- **Non theophylline use [C]**
- **The primary outcome: AKI**

  Secondary outcome measures: change in SCr level, need for dialysis, and in-hospital mortality [O]

Systematic review worksheet

Is it unlikely that important, relevant studies were missed 沒有遺漏重要的文獻？

☐是	■否	☐ 不清楚
評論： Meta-analysis of randomized controlled trials using MEDLINE (1966 to July2011), EMBASE (1980 to July 2011), Web of Science (1986 to July 2011), the Cochrane Central Register of Controlled Trials (1996 to July 2011), without language restriction.		

Were the criteria used to select articles for inclusion appropriate 選擇文獻的準則適當?

■是	□ 否	□ 不清楚
評論： Inclusion criteria: (1)randomized controlled trials (2) the intervention was adenosine receptor antagonists (3) the incidence of contrast-induced AKI (4) did not restrict eligibility according to kidney function.		

Were the included studies sufficiently valid for the type of question asked

選擇的文獻有效回答所問的問題?

■是	□ 否	□ 不清楚
評論： Summary: theophylline treatment significantly decreased the incidence of contrastinduced AKI and had a modest improvement on kidney function after contrast exposure in the general population. However, beneficial effects of theophylline were not observed in patients with high baseline SCr values (SCr 1.5 mg/dL)		

Were the results similar from study to study
各研究的結果相似?

□是	■否	□不清楚
評論： - potential sources of heterogeneity: moderate (I^2–squared = 44.3%) . SCr level . Theophylline dose, routine, combined with NAC . Jadad score		

Table S2 Univariate Meta-regression Analysis of Possible Sources of Heterogeneity

Possible Source of Heterogeneity	Scale	Proportional Change of Risk Ratio (95% CI)*	P Value
Number of patients	Per 100-patient increment	0.62 (0.27-1.41)	0.3
Mean age	Per 1-year increment	1.06 (0.99-1.13)	0.1
N-acetylcysteine	Yes or no	0.39 (0.07-2.36)	0.3
Intraarterial administration of contrast only	Yes or no	0.94 (0.27-3.25)	0.9
High-osmolar	Yes or no	0.16 (0.016-1.73)	0.1
Dose of contrast media	Per 100-mL increment	1.25 (0.26-6.17)	0.8
Hydration	Yes or no	1.83 (0.56-5.92)	0.3
Mean serum creatinine	Per 1-mg/dL increment	6.95 (2.12-22.8)	0.001
Proportion with diabetes	Per 1% increment	1.00 (0.97-1.03)	0.8
Intention-to-treat analysis	Yes or no (or not specified)	0.46 (0.14-1.58)	0.2
Allocation concealment	Yes or no (or not specified)	12.8 (0.50-327.26)	0.1
Blinding	Yes or no (or not specified)	1.92 (0.49-7.61)	0.4
Adequacy of randomization	Yes or no (or not specified)	3.79 (1.05-13.63)	0.04
Jadad score	Per 1-score point increment	2.44 (1.52-3.92)	<0.001

* Results were presented with exponentiated regression coefficients and their 95% CIs for every 1-scale increase between each factor as relative risk for treatment with theophylline on contrast-induced acute kidney injury, with values >1.0 indicating less effectiveness of the theophylline regimens.

APPLY

結合醫學倫理方法

將**study**的結果應用在病人身上

醫療現況	病人意願
使用無確切證據的處置會被健保局核刪	若確實對預後有幫助，病人及家屬皆願意配合
生活品質	社會脈絡
若能使顯影劑對腎功能影響到最低，對於未來的生活品質有正面價值	若有更佳的預防顯影劑對腎功能影像的方式，事前若未對家屬或病人提起，事後若真的發生後遺症可能會被家屬或病人質疑

將**STUDIES**的搜尋結果應用到我病人身上

- 此篇system review可發現theophylline可大大降低contrast induced AKI的incidence，但若serum creatinine原本就大於等於1.5以上，則效果不明顯，未達統計上的意義

總結與討論

- 根據此篇paper以及其他資料， theophylline在預防contrast-induced nephropathy的效果以統計結果來看，確實可以降低contrast induced nephropathy，雖然所分析的RCT中的heterogeneity高，但有可能是因爲一開始病人的serum creatinine指數不同，太高其實theophylline的統計結果就無特別療效。
- 我們的病人由於一開始就發生acute kidney injury，根據此篇結果，其實使用theophylline效果並不明顯，因此我們的病人沒有服用theophylline

Thank you for your attention!