Evidence-based Medicine

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101.6.18

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

- Name: 劉郭X珠
- Chart No.: 25050621
- Sex: Female
- Age: 56 y/o

Present Illness

- a patient of hepatitis B with liver cirrhosis
- transfered to our Chest surgery OPD due to progressive dyspnea from right pleural massive effusion
- 98/2/13 thoracocentasis with pigtail insertion in OPD
  - chylothorax (TG up to 138mg/dl)
  - daily drainage about 1000ml

- 2/20 CXR showed hydropneumothorax
  - dislocation of tube was impressed
  - the tube was re-inserted
- 2/24 ER
  - fever , progressive dyspnea, productive cough
  - elevated CRP (182 mg/L)
  - CXR revealed right pleural effusion
    - chest tube was isnerted


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Hospitalization Course

- massive fluid from pig-tail and chest tube was noted
- lymphoscintigraphy: suspect thoracic duct leakage and chylothorax is highly suspected
  - NPO and TPN supply
  - consider operation for thoracic duct repair
- pancytopenia was noted
  - bone marrow aspiration: hypercellular marrow with erythroid hyperlplasia
  - prescribe prednisolone

- patient and family asked for discharge
- chest tube was removed
- discharged on 3/24

Asking-

Background Question

Q1. What's the etiology of chylothorax?
Q2. How to diagnose chylothorax?
Q3. How to treat chylothorax?

Q1. What's the etiology of chylothorax?

Reference:

UpToDate.

Etiology of chylothorax

Etiology	Number of cases[1] (percent)	Number of cases[2] (percent)
Nontraumatic	138 (72)	34 (46)
Malignant	87 (45)	13 (18)
Lymphomatous	70 (37)	9 (12)
Nonlymphomatous (primary pulmonary, mediastinal, metastatic extrathoracic malignancies)	17 (9)	4 (5)
Nonmalignant	51 (27)	21 (28)
Idiopathic	26 (14)	7 (9)
Miscellaneous (benign tumors, lymphangioleiomyomatosis, intestinal lymphangiectasis, protein-losing enteropathy, regional ileitis, reticular hyperplasia, pleuritis, cirrhosis, thoracic aortic aneurysm, lupus, tuberculosis, sarcoidosis, amyloidosis, venous thrombosis, mitral stenosis, nephrosis, thyroid goiter, tuberous sclerosis, filariasis, heart failure, Down syndrome, Noonan syndrome)	15 (8)	14 (19)
Traumatic	53 (28)	40 (54)
Surgical (cardiovascular, aortic, thoracoplasty, esophagectomy, lobectomy, pneumonectomy, Bochdalek herniorrhaphy, transabdominal vagotomy, venous catheterization, esophageal endoscopic sclerotherapy, neck surgery)	48 (25)	40 (54)
Nonsurgical (penetrating or nonpenetrating trauma to the neck, thorax, and upper abdomen, straining, coughing, yawning, vomiting)	5 (3)	

References:

1. *Valentine VG, Raffin TA. The management of chylothorax. Chest 1992; 102:586.*
2. *Doerr CH, Allen MS, Nichols FC 3rd, Ryu JH. Etiology of chylothorax in 203 patients. Mayo Clin Proc 2005; 80:867.*

Q2. How to diagnose chylothorax?

Gold Standard

Reference:

UpToDate.

- demonstration of chyle leakage by **direct visualization or lymphangiography**
  - However, cases have been described where the fluid characteristics suggest chylothorax, but leakage is not confirmed as it is too slow or diffuse to visualize.

Pleural Fluid Analysis

Reference:

UpToDate.

- cell count and differential
- pH
- **triglycerides, cholesterol**, glucose, lactic dehydrogenase (LDH), total protein
- cytology
- microbiologic smear and culture

Lipid Analysis

Reference:

UpToDate.

- A pleural fluid triglyceride concentration **greater than** **110 mg/dL** strongly supports the diagnosis, and a level less than 50 mg/dL excludes a chylothorax with reasonable likelihood.
- between 50 and 110 mg/dL
  - lipoprotein electrophoresis of the pleural fluid
  - chylomicrons in the pleural fluid
- cholesterol level : generally less than 200 mg/dL

Q3. How to treat chylothorax?

Reference:

UpToDate.

- The optimal management of a chylothorax is **unclear** because no prospective studies exist to guide therapy.
- Our treatment approach is based on clinical experience and data from case reports and case series.
- The exact steps vary depending on the etiology of the chylothorax, the rate of accumulation, local expertise with various procedures, and the response to initial therapy.

Nontraumatic

Malignant chylothorax

Reference:

UpToDate.

- Initial treatment
  - therapeutic **thoracentesis** for relief of dyspnea
  - treatment of the underlying malignancy with chemotherapy and irradiation
- If failure
  - instillation of a pleural sclerosing agent (such as talc) through a chest tube or thoracoscope
  - malignant chylothorax does not usually benefit from ligation of the thoracic duct

Reference:

UpToDate.

- still failure
  - depending on local expertise, such as the long-term use of an indwelling pleural catheter or placement of pleuroperitoneal or pleurovenous shunts
  - subcutaneous octreotide and a fat-free diet

Idiopathic and benign chylothorax

Reference:

UpToDate.

- Initial
  - treat underlying disease
  - chest tube drainage
  - dietary control
    - more slowly accumulating:
      - high protein-reduced fat oral diet first
      - if failure, fasting and total parenteral nutrition
- Conservative measures are successful in approximately 40 to 80 percent.

Reference:

UpToDate.

- If persists for more than two weeks despite these measures, or sooner if the fluid output exceeds 1 L/day
  - chemical pleurodesis, decortication, oversewing of the thoracic duct disruption and any leaking collaterals, and also ligation of the thoracic duct at the aortic hiatus
  - the highest likelihood of success: **thoracic duct ligation with talc pleurodesis** at the time of video-assisted thoracoscopy
  - decortication for patients who have failed prior thoracic duct ligation and pleurodesis

Foreground Question

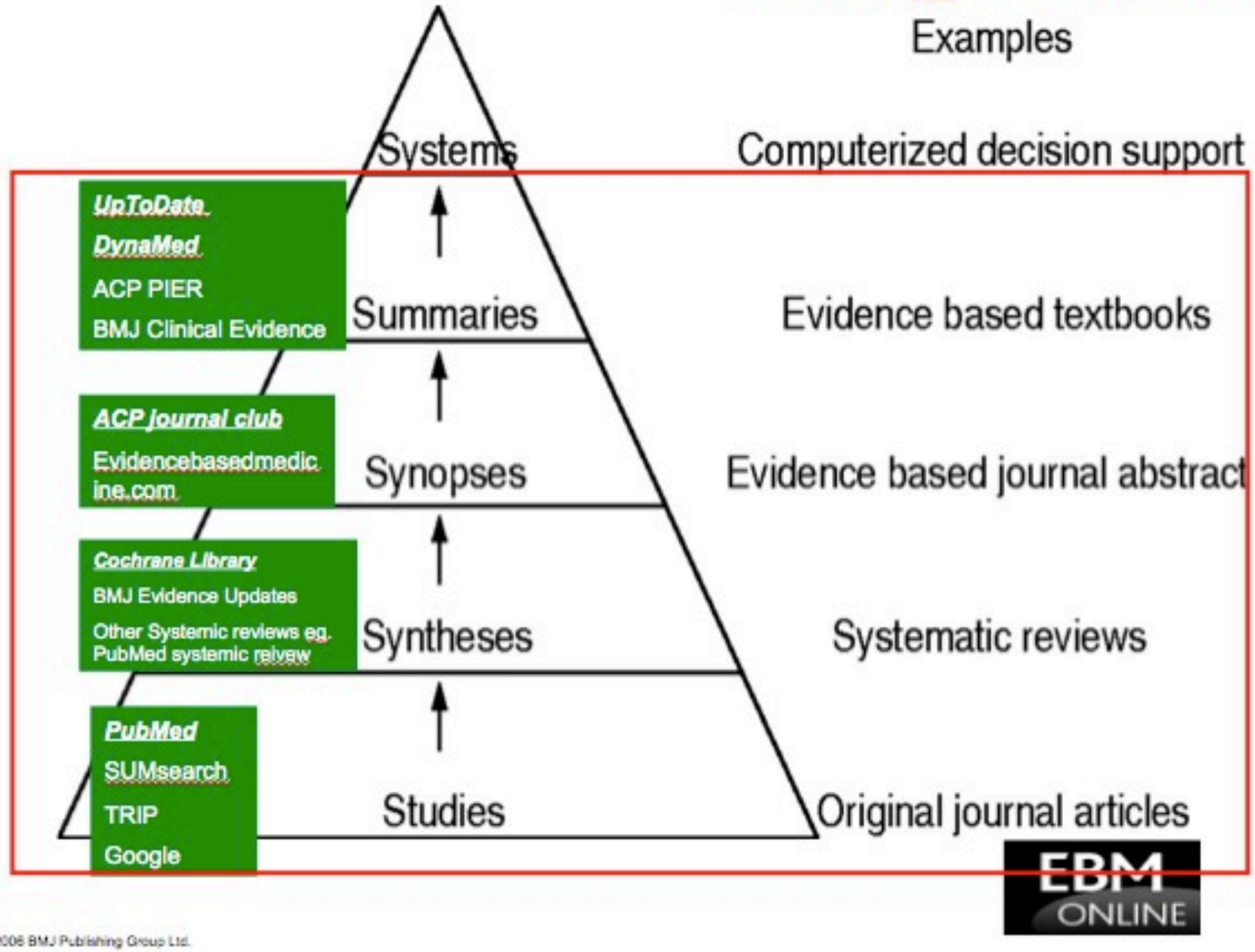
PICO

Is conservative therapy better than early surgical intervention for patients with nontraumatic chylothorax?

Patient	Patients with nontraumatic chylothorax
Intervention	conservative therapy
Comparison	early surgical intervention
Outcome	resolution of chylothorax
Time	days

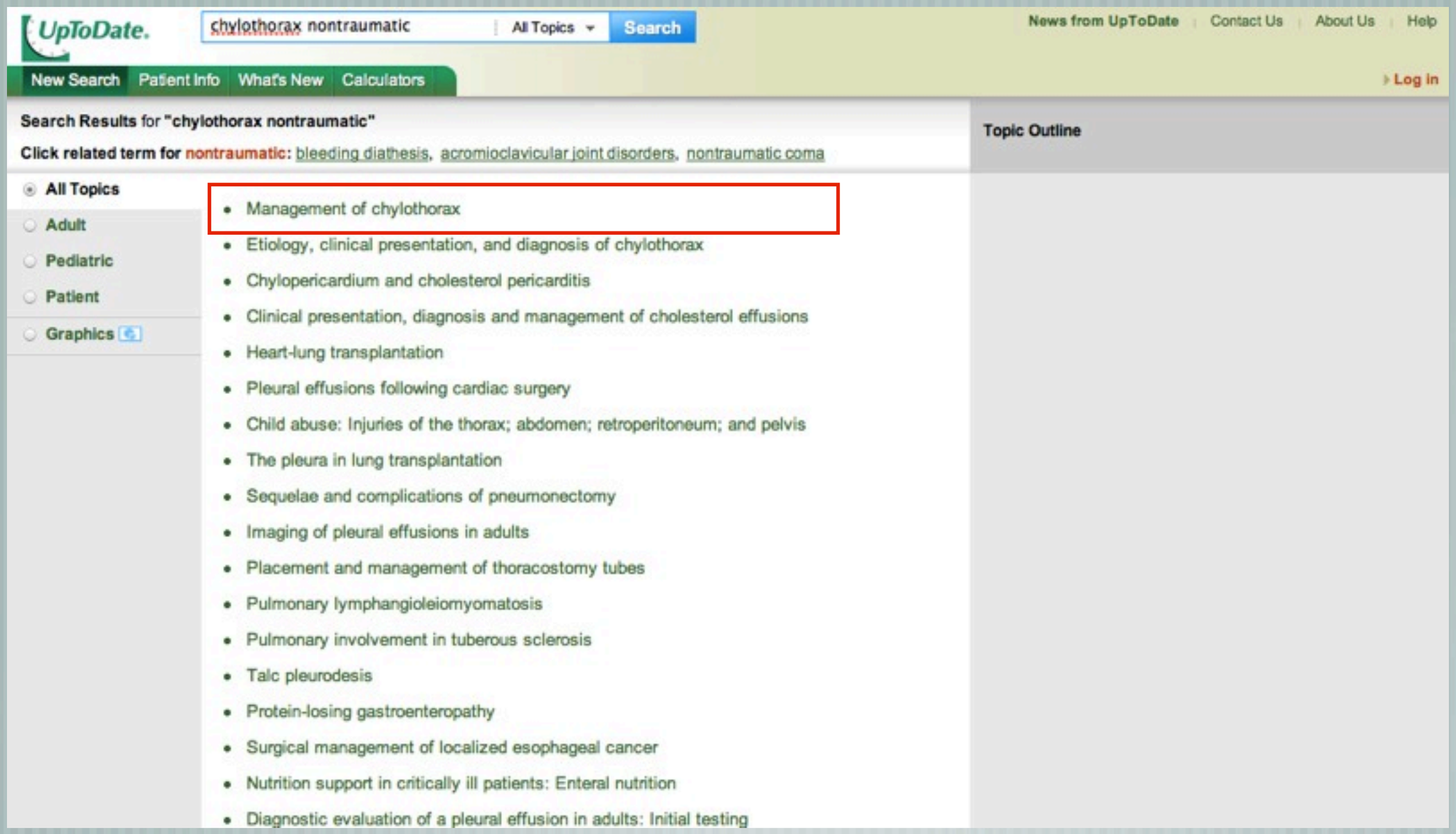
The "5S" levels of organisation of evidence from healthcare research

Brian Haynes, R Evid Based Med 2006;11:162-164



搜尋UpToDate

Key words: chylothorax, nontraumatic



搜尋ACP journal club

keyword: chylothorax

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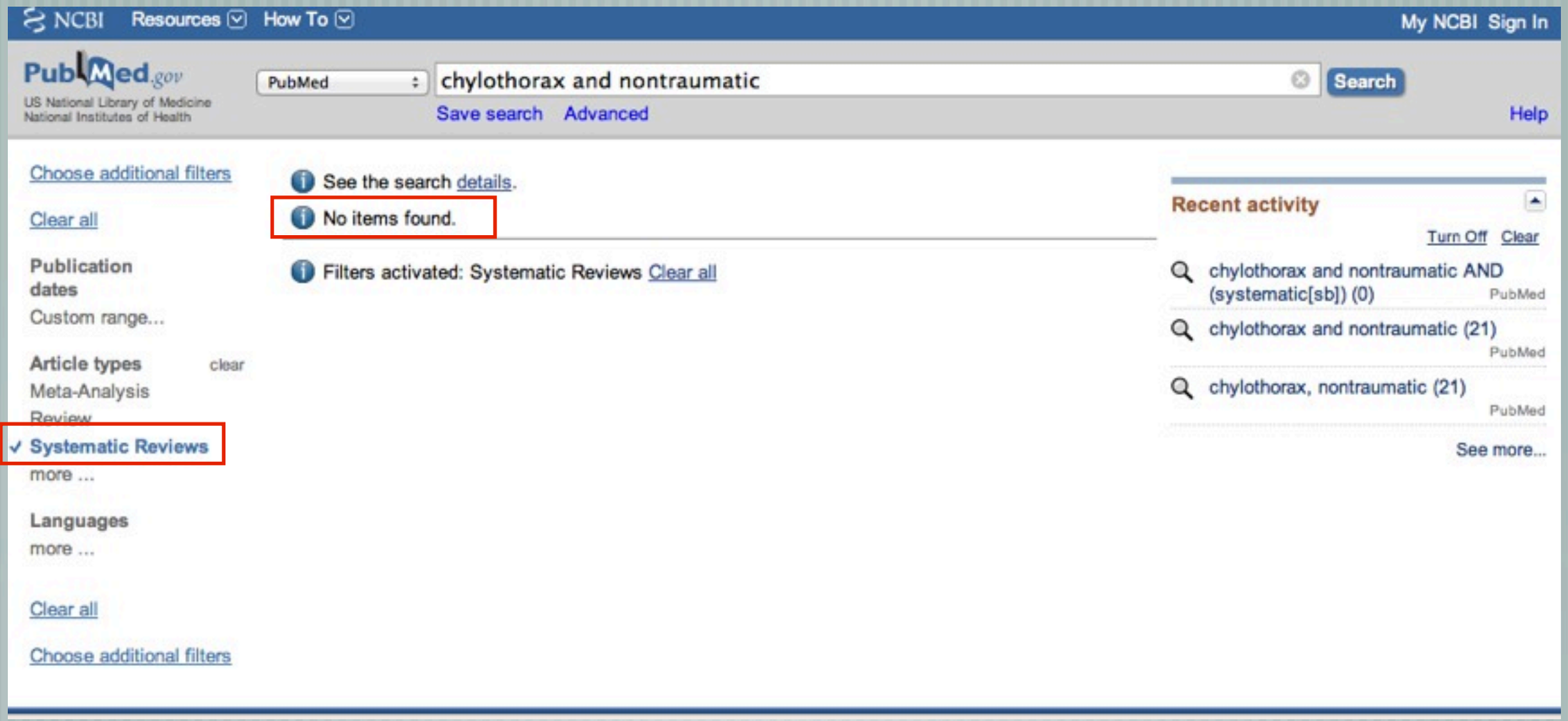
- Make sure all words are spelled correctly.
- Try different keywords.
- Try more general keywords.

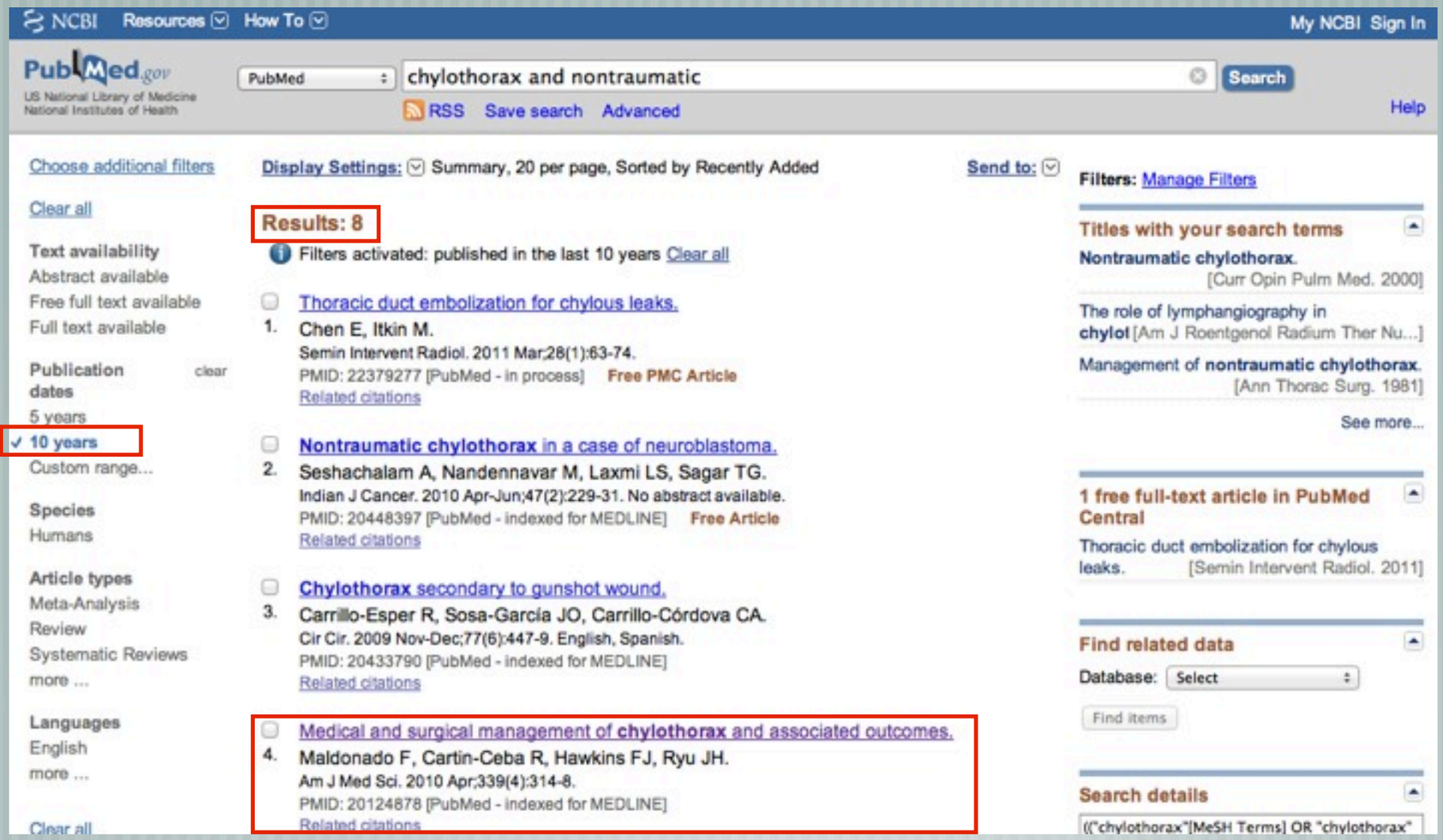
搜尋PubMed-systemic review

Key words: chylothorax, nontraumatic



搜尋PubMed-studies

Key words: chylothorax, nontraumatic



Medical and Surgical Management of Chylothorax and Associated Outcomes

Fabien Maldonado, MD, Rodrigo Cartin-Ceba, MD, Finn J. Hawkins, MBBCh and Jay H. Ryu, MD

The American Journal of the Medical Sciences • Volume 339, Number 4, April 2010

Background

- Differing management strategies have been described over the years.

- Although attempts at a more systematic approach to treating chylothorax have been presented, the evidence for such recommendations remains scarce, including the absence of controlled clinical trials, largely because of **the uncommon occurrence** of this disorder.

- <u>prolonged</u> chylous fluid drainage
  - malnutrition
  - immunocompromised state
  - severe electrolyte abnormalities
- potentially contributing to **<u>increased morbidity and mortality</u>**

METHODS

Study Subjects

- retrospective, single-center study
- computer-assisted search of electronic medical records at the Mayo Clinic, Rochester, MN
- January 1, 1997 - December 31, 2006
- 74 adult patients (≧18 years old)
  - presence of chylomicrons in the pleural fluid

Clinical Data

- Medical records were carefully examined and retrieved.
- **Success** in the management of chylothorax was defined by resolution of the pleural effusion without documented recurrence in the follow-up period.

Statistical Analyses

- continuous data
  - Wilcoxon rank-sum test
- categorical variables
  - chi-squared test or Fisher exact test
- a P-value≦ 0.05 was considered significant (2-tailed)

RESULTS

General Data

- 37 men (50%) and 37 women (50%)
- median age: 61.5 years (range, 20–93 year)
- right hemithorax: 39 patients (53%)
  left hemithorax: 19 patients (26%)
  bilateral: 16 patients (22%)
- traumatic (surgery or invasive procedure) : 40 (54%)
  nontraumatic or idiopathic: 34 (46%)

- traumatic group
  - 39 post-surgery (mostly esophageal, pulmonary, or cardiac)
  - 1 thrombosis of a central vein after CVC

- Nontraumatic causes
  - 9 lymphoproliferative disorders
  - 5 portal hypertension from cirrhosis or pancreatic cancer
  - 3 radiation-related injuries
  - 3 primary lymphatic disorders
  - 3 solid tumors
  - 2 thoracic duct obstruction from subclavian thromboses (idiopathic and secondary to thoracic outlet syndrome)
  - 1 lymphangioleiomyomatosis
  - 1 amyloidosis

No cause was identifiable in 7 cases.

Traumatic Chylothorax

TABLE 1. Initial interventions and associated outcomes for patients with traumatic chylothorax (n = 40)

Mode of management	No. patients (%)	Success rate (%)
Dietary measures only[a]	4 (10)	50
Thoracentesis only	3 (8)	66
Dietary measures and thoracentesis	2 (5)	50
Chest tube drainage alone	3 (8)	67
Dietary measures and chest tube drainage	23 (58)	43
Dietary measures and surgical pleurodesis	1 (3)	100
Thoracic duct ligation	1 (3)	100
Surgical pleurodesis and thoracic duct ligation	3 (8)	33
Overall	40 (100)	50

[a] One of these patients also received octreotide therapy.

initial conservative therapy: 88%

success rate: 49%

early surgical intervention: 12%

success rate: 60%

TABLE 2. Outcomes associated with surgical interventions for traumatic chylothorax (n = 25)

Mode of management	No. patients (%)	Success rate (%)
Talc pleurodesis alone	1 (4)	100
Mechanical and talc pleurodesis	1 (4)	0
Thoracic duct ligation alone	5 (20)	100
Thoracic duct ligation and mechanical pleurodesis	4 (16)	75
Thoracic duct ligation and talc pleurodesis	12 (48)	100
Thoracic duct ligation and pleurectomy	2 (8)	100
Overall	25 (100)	92

62.5%

Nontraumatic Chylothorax

TABLE 3. Initial interventions and associated outcomes for patients with nontraumatic chylothorax

Type of initial treatment	No. patients (%)	Success rate (%)
Observation only[a]	3 (9)	33
Thoracentesis	21 (62)	24
Chest tube drainage	2 (6)	0
Pleurodesis	3 (9)	33
Pleurodesis and thoracic duct ligation	4 (12)	50
LeVeen shunt	1 (3)	0
Overall	34 (100)	27

[a] One of these 3 patients received chemotherapy for the treatment of underlying lymphoma and had resolution of chylothorax.

at least 3 thoracentesis after the diagnosis of chylothorax established

early surgical intervention : 24%
success rate: 37.5%

TABLE 4. Outcomes associated with surgical interventions for nontraumatic chylothorax (n = 19)

Mode of management	No. patients (%)	Success rate (%)
Talc pleurodesis alone	5 (26)	80
Thoracic duct ligation alone[a]	1 (5)	0
Thoracic duct ligation and mechanical pleurodesis	2 (11)	50
Thoracic duct ligation and talc pleurodesis	8 (42)	88
Thoracic duct ligation with mechanical and talc pleurodesis	1 (5)	0%
Thoracic duct ligation and pleurectomy	1 (5)	100
LeVeen shunt	1 (5)	0
Overall	19 (100)	68

[a] The patient who underwent thoracic duct ligation alone eventually underwent palliative placement of an indwelling pleural drainage catheter for malignant pleural effusion with metastatic adenocarcinoma.

56%

- 2 patients with cirrhosis underwent liver transplantation with prompt resolution of chylothorax and chylous ascites.
- Two other patients with cirrhosis expired before transplant:
  - 1 had resolution of the chylothorax after talc pleurodesis (but persistence of chylous ascites)
  - another had persistence of his chylothorax despite a transjugular intrahepatic portosystemic shunt.

- <u>Reaccumulation or persistence</u> of chylothorax occurred in 17 patients (**<u>50%</u>**).
  - 6 died (3 from malignancy, 1 from respiratory failure, and 1 from complications of cirrhosis and 1 for unclear reasons)
  - 2 complete resolution after liver transplant
  - 1 complete resolution after chemotherapy for lymphoma
  - 3 stable effusions without clinical consequences
    - 1 LeVeen shunt, unsuccessful
    - 1 bilateral subclavian stents, unsuccessful
  - 5 loss follow-up

Comparison of Traumatic and Nontraumatic Groups

- A surgical procedure was eventually performed in 44 of 74 patients (59%), with a rate that was similar between traumatic and nontraumatic groups (62% and 56%, respectively).

- rate of resolution with initial management
  - nontraumatic VS traumatic (27% versus 50%, P=0.048)

- recurred or persisted
  - nontraumatic VS traumatic (50% versus 13%, P<0.001)

DISCUSSION

- Chylothorax is an uncommon form of pleural effusion and a rare complication of thoracic surgical procedures (**0.5%** of the cases).

- Once the diagnosis of chylothorax is established, decisions regarding additional diagnostic evaluation and management are difficult to establish because no evidence-based guidelines addressing these issues exist.

Traumatic Chylothorax

- Most authors have recommended an initial attempt at a conservative approach consisting of chest tube drainage and dietary measures.
- Conservative measures have been shown to be less effective in high-volume drainage (>1000 mL/d for ≧7 days) and after esophageal surgeries.

The initial approach chosen, whether surgical or conservative, resulted in resolution of the chylothorax in half of the patients. There was **no significant difference in rates of success** whether the initial mode of management was medical or surgical although the analysis was limited by the modest number of subjects and the retrospective nature of the study.

- Based on available data, it seems reasonable to recommend an **initial trial of medical measures** for several days, before advancing to more invasive options.

- Eventual resolution can be achieved in most patients with traumatic chylothorax with treatment measure that may include surgical maneuvers in more than one half of these patients.

Although no guidelines exist and surgical practices vary widely, the general consensus suggests an initial conservative approach followed by surgical management if needed.

Because the mortality rate of untreated chylothoraces seems to be particularly high in patients who have undergone esophageal operations, **early reoperation** has been recommended for these patients.

Nontraumatic Chylothorax

- Optimal management of nontraumatic chylothorax is even more difficult to determine, because there exists a wide spectrum of medical disorders associated with the development of chylothorax.

- Although treatment of the underlying disease is often recommended as the definitive treatment of nontraumatic chylothorax, the effectiveness of this approach is **unclear** and may vary widely depending on the underlying disease and the clinical context.

Our data suggest that medical management of nontraumatic chylothorax leads to resolution in only a **minority** of cases.

The majority (62%) of our patients with nontraumatic chylothorax were initially treated with periodic thoracenteses, with a resolution rate of only 19%.

- Treatment of the underlying cause seems reasonable whenever possible, but a substantial portion of patients incorporation are left with persistent effusion.

- Despite incorporation of surgical maneuvers in their management, nearly **one third** of patients with nontraumatic chylothorax may **fail** to achieve resolution of their chylothorax.

CONCLUSIONS

Nonsurgical approaches may lead to resolution of the chylothorax in nearly one half of patients with traumatic chylothorax but in only a minority of those with nontraumatic chylothorax.

The majority of patients with **nontraumatic** chylothorax will **eventually require surgical maneuvers**, but one third of such patients fail to resolve their chylothorax.

Appraisal

AAMPICOT將文獻分析

Item	AAMPICOT for therapy criteria	Comments
Answer	此文獻有沒有回答我的問題	部分
Authors	作者群是這領域的專家嗎?	是
	有沒有利益衝突	沒有
Method	本文獻研究設計是屬於以下哪一類SR, RCT, Cohort, Case-control, Case series or report, Expert opinion	cohort
Population	取樣是否為隨機取樣?	否
	取的樣本是否具代表性? 其特性是否接近我的病人?	是
	分組是否是隨機分組?	否
	分組是否採用盲法?	否

Intervention	給予實驗組的處置是否描述清楚，並且是臨床可行的?	是
Comparison	對於對照組的處置是否描述清楚，並且是臨床可行的?各種可能比較皆有了?	是
Outcome	測量了哪些結果?是某用可觀的方式測量?	resolution, recurrence or persistent of chylothorax
	這些結果是否有統計學上的重要性?	是
	這些結果是否有臨床上的重要性?	是
	是否呈現結果的「數值」，「p值」，「信賴區間」，「檢力」？	是
Time	測量結果的時間點是否合宜？	是
	追蹤時間是否夠長？	是
	文獻發表時間？	2010

Apply

結合醫學倫理方法
將study的結果應用在病人身上

總結與討論

- 目前研究證據不足，但依據目前的研究及經驗，conservative therapy對這類病人的效果不好，加上大量的pleural fluid流出，可能造成病人營養流失，免疫力變差，可考慮早期手術介入。

Thanks for your attention!!