出國報告(出國類別：參加國際會議)

2011 年美國胸腔學會國際年會

服務機關：國防醫學院三軍總醫院
姓名職稱：張 宏、主治醫師
派赴國家：美國
報告日期：100 年 5 月 25 日
出國時間：100 年 5 月 12 日至 5 月 20 日

一、 摘要：

參加美國胸腔學會國際會議主要的目的是展示“探討硫辛酸對內毒素合併呼吸器誘發肺損傷之保護影響”，藉此機會與世界頂尖及相關領域的學者專家交流並接受指正且尋求研究議題。並且參加研究課程且吸收新知及世界潮流的動向。期望對於肺癌、慢性阻塞性肺部疾病及肺容積縮減手術有進一步的認識及瞭解。

參加 2011 年美國胸腔國際會議出國報告目錄

二、 本文：

1. 目的： 參加美國胸腔學會國際會議主要的目的是展示“探討硫辛酸對內毒素合併呼吸器誘發肺損傷之保護影響”，藉此機會與世界頂尖及相關領域的學者專家交流並接受指正且尋求研究議題。並且參加研究課程且吸收新知及世界潮流的動向。期望對於肺癌、慢性阻塞性肺部疾病及肺容積縮減手術有進一步的認識及瞭解。

2. 過程： 2011 年 5 月 12 日飛去美國丹佛完成報到手續參加美國胸腔學會國際會議。

100	5 月	12 日	從臺灣桃園國際機場搭長榮航空 BR 0012（5/12 18:40）於 15:25 抵達美國洛杉磯轉機； ②從美國洛杉磯搭美國聯合航空UA 0364（5/12 18:43）於 22:00 抵達美國丹佛
100 年	5 月	13 日	大會報到、參加研究研討會
100 年	5 月	14 日	開幕式及 ATS Meet the Professor Seminars
100 年	5 月	15 日	參加年度回顧、臨床追踪主題、危重病急救軌道、張貼 poster
100 年	5 月	16 日	多樣性論壇、講座教授拜訪、系列專題講座、會員大會會議等研究研討會
100 年	5 月	17 日	參加系列專題講座、年度回顧、總統的演講 /會員大會等研究研討會
100 年	5 月	18 日	①參加系列專題講座、外組會議等研究研討會、大會結束 ②從美國丹佛搭美國聯合航空UA 0595（5/18 18:51）於 20:36 抵達美國舊金山轉機
100 年	5 月	19 -20 日	從美國舊金山搭長榮航空 BR 0017（5/19 01:40）於 5/20 05:50 返抵臺灣桃園國際機場

3. 心得：

- 研究顯示輔助性化學治療對於Ⅱ，ⅢA 非小細胞肺癌有治療效果，對於 stage IB 確無定論。生物標記(markers of prognosis and predicton of

response)可能可以區分及篩選出輔助性化學治療有效果及反應的病患，作者 Ehu C 在 JBR.10 研究計畫中收集 133 個 stage IB and 及Ⅱ的肺癌檢體做了 gene expression profiling 此 133 病患隨機分成 Vinorelbine /cisplatin 及 observation 組。Prognostic gene expression signature 從 62 個觀察組存活著當中製作出，再次用 RT-PCR 方法加以證實並且在 4 個 independent microarray data sets 作測試發現 15 個 gene 和癌症期別有關的 prognostic signature 有足夠能力能區別出高低肺癌復發期群的病患，輔助性化學治療能延長 High risk groups 的存活率，但對 low risk group 沒有助益，但對於 stage IB 或 Stage Ⅱ high risk group 也有 benefit.
molecular characterization. prognostic and predictive gene signature for adjuvant chemotherapy in resected non-small cell lung cancer. J clin Dncol 2010:28:4417-24

- 吐氣末正壓呼吸於急性肺損傷及急性呼吸窘迫症的應用 PEEP in ALI/ARDS
  Higher Vs Lower positive End-Expiratory pressure in patients with acute lung injury and Acute respiratory Distress syndrome: systemic review and meta-analysis. JAMA 2010:303:865-93
  ALVEOLI、EXPRESS 及 LOVS 三大隨機臨床試驗比較高低吐氣末正壓呼吸對於急性肺損傷及急性呼吸窘迫症的治療效果，於 2299 病患中，Higher 及 lower PEEP 病患 baseline 相似，整體死亡率於兩組相似，higher PEEP 於 ARDS 存在或不存在時有不同治療效果，higher PEEP 這組較不需使用 rescue therapy ，縱使運用 rescue therapy 也有較低死亡率，作者總結 Higher Vs lower PEEP 和 improved hospital survival 沒有相關，但會 improve ARDS 病人的 Outcome

- Early Vs late Tracheotomy for prevention in mechanically Ventilated Adult ICU
  patients: A Randomized controlled trial. JAMA.2010:303:1483-9
  在此隨機控制的臨床研究中，作者探討作氣切的時間是否會影響呼吸機伴隨肺炎的產生(Ventilator associated pneumonia. VAP) 600 位病患接受呼吸機通氣 24 小時以上並且有 moderate SAPSⅡscores 及 multi-organ dysfunction score 大於 5 分被收錄 419 位病患 48 小時後根據 standard criteria 沒有進步或變壞隨機分成二組，一組是 6 至 8 天在氣管插管後，另一組是 13 天至 15 天接受 percutaneous tracheostomy 在 early group 69% 病患接受氣切，57% late group 接受氣切，early tracheostomy 似乎可以減少 VAP 但沒有達成統計學上的意義，但 early tracheostomy 不會減少 28 天死亡率，一年死亡率及 length of hospital stay 作者總結 early tracheotomy 不會減少 VAP 的機率

- Lung cancer treatment

Ana plastic lymphoma kinas inhibition in non-small cell lung cancer. N Engl J

med 2010:363:1693-703

EML4-ALK 是 aberrant 融合基因會於 2-7%非小細胞肺癌發現。它 encodes a chimeric cytoplasmic protein 並持續有 kinase activity. 它常發現於年輕男性併有輕微抽菸的病史並且有肺腺癌的病患。EML4-ALK 融合基因的腫瘤不會含有 EGFR mutation 及 MET amplification ALK protein 會驅動肺癌細胞的增生。Crizotinib 是口服 ALK 及 MET tyrosine kinases ATP 競爭選擇型抑制劑，在 open-label phase I trial 在 2 病患俱有非小細胞肺癌對 crizotinib 反應相當良好。在收集了 82 個晚期肺癌的病患，FISH Test 顯示腫瘤含有 ALK positive gene 且 ECOG performance status 0-2，接受 crizotinib overall response rate 是 57%，progression free survival 6 個月後是 72%，噁心、腹瀉及視力障礙是主要的副作用。

4. 建議：

1、由於研究實驗需投入心血耗時損力，希望能全額補助參展者以鼓勵良好基礎及臨床醫學之研發。
2、對於特定課程 (Postgraduate Course)新知教授亦能給予補助。

投稿摘要如下

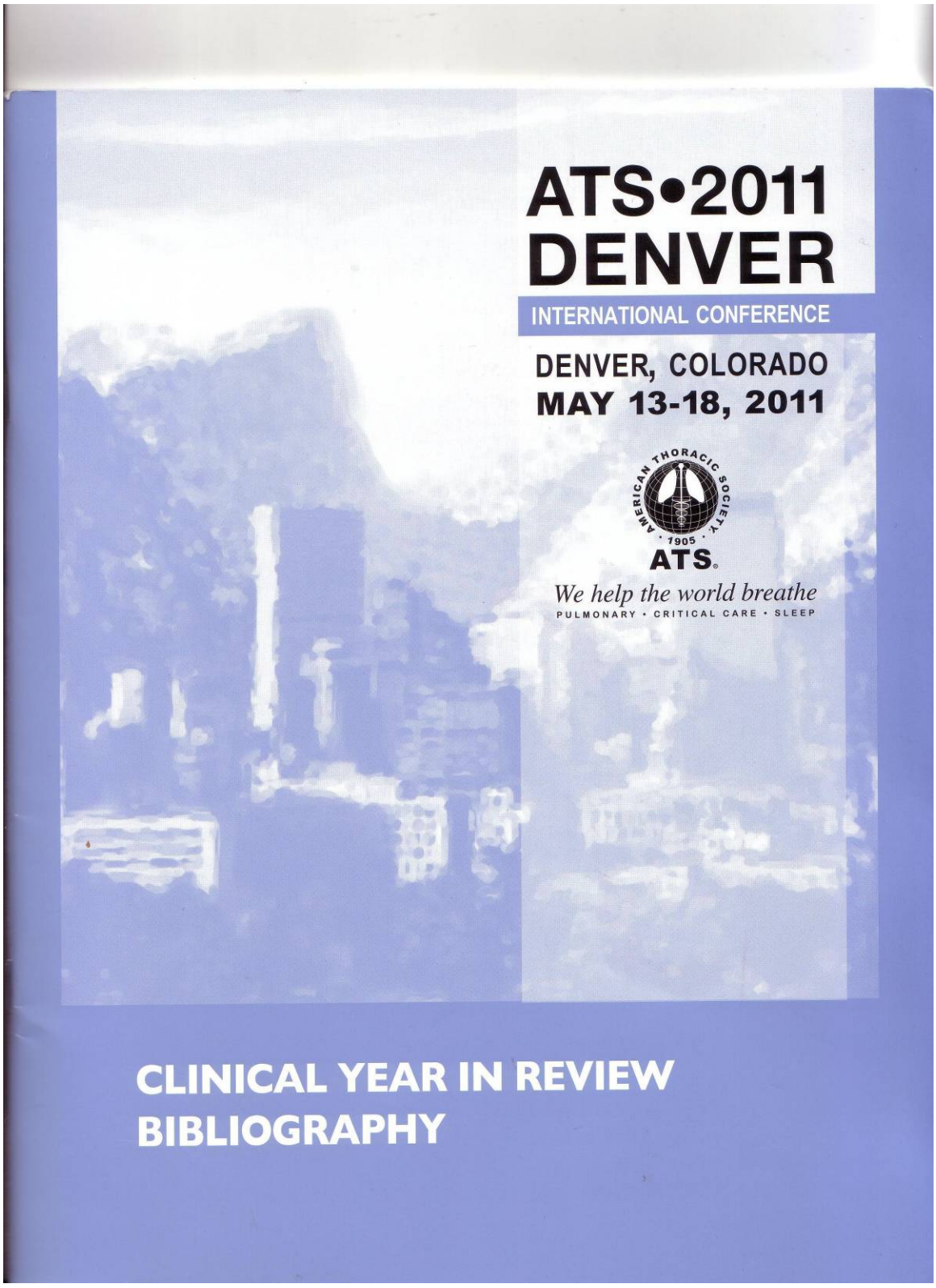
目的: 呼吸器常用於呼吸衰竭的病人，若不適當使用或長時間給予呼吸器，皆易造成肺部損傷，並引發大量發炎物質的釋放，稱之呼吸器誘發肺損傷 (Ventilator-induced Lung Injury, VILI)。過去已有文獻指出，單獨給予低中度潮氣容積並不會導致肺損傷，但如合併一些刺激物質如：內毒素、油酸、鹽酸等，則會誘發肺部損傷，故本研究主要模擬臨床上有肺部疾病的病人長時間給予呼吸器且合併有感染發炎情況下所造成的肺損傷之動物模式下行一系列研究。以往研究已發現，在此呼吸器誘發肺損傷動物模式中會增加自由基生成，進而造成肺組織傷害。因此，或許可藉由使用具降低氧化壓力之藥物以改善肺損傷情形。硫辛酸 (α-lipoic acid, ALA) 是一種存在於粒線體的輔酶，具有多種細胞保護作用，可明顯改善氧化壓力所造成的相關疾病。本研究目的主要在探討內毒素合併呼吸器所誘導肺損傷模式中，評估給予硫辛酸是否有保護效果並探討相關機制。

方法: 本實驗設計爲於實驗前一小時投予硫辛酸 (25,50,100 mg/kg, i.p.)，之後再於氣管內滴入內毒素 (2 mg/kg)，並設定潮氣容積 (V_T):20 ml/kg，每分鐘 60 次呼吸次數，在第 3 小時將動物犧牲及評估肺損傷程度。

結果: 實驗結果顯示，硫辛酸 (100 mg/kg) 可顯著減少支氣管肺泡灌洗液中蛋白質濃度、白血球數目、細胞激素 (tumor necrosis factors-α, TNF-α；intreleukine-1β, IL-1β ；intreleukine-6, IL-6) 及趨化激素 (macrophage inflammatory, MIP-2)，且可減少肺組織中肺組織濕/乾重量比、骨髓過氧化酶 (myeloperoxidase, MPO) 活性、丙二醛 (Malondialdehyde, MDA) 生成量，並降低 COX-2 蛋白質表現量。同時，也明顯改善肺臟病理組織變化。此外，本實驗也發現硫辛酸 (100 mg/kg) 顯著減少肺組織中超氧游離基 ($O_2^{\cdot-}$) 含量及抑制肺組織 iNOS、XBP1、ASK1、p38、CHOP 等表現，但可增加 HO-1 和 GRP78 基因表現量，導致 caspase-3 蛋白質表現量減少，降低細胞走向細胞凋亡路徑。

結論: 因此，我們推論硫辛酸可能是經由減少細胞激素、趨化激素釋放與降低發炎性基因表現及自由基生成，使內質網壓力相關因子及細胞凋亡被抑制但增加 HO-1 及 GRP78 基因表現，而達到預防呼吸器誘發肺損傷的療效。

參. 附錄：參加會議之資料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EPIDEMIOLOGY

Raji OY, Agbaje OF, Duffy SW, Cassidy A, Field JK. **Incorporation of a genetic factor into an epidemiologic model for prediction of individual risk of lung cancer: The Liverpool Lung Project.** Cancer Prev Res 2010;3: 664-9.

Summary
The Liverpool Lung Project (LLP) previously developed and validated a predictive model for 5-year absolute risk of developing lung cancer. Five epidemiologic factors were included in the model – smoking duration, previous diagnosis of pneumonia, prior diagnosis of a malignant tumor, occupational exposure to asbestos, and a family history of lung cancer. The Sequenom-Genefinder project identified and validated a SNP in the SEZ6L gene as a modifier of lung cancer risk. A subset of 200 lung cancer subjects and 188 age and sex matched control subjects from the LLP had been genotyped in the validation phase of the Genefinder study. Ten percent of those with lung cancer and 3% of the controls were found to have the homozygote mutant genotype (p=0.02). There was no confounding effect of the SEZ6L SNP on the relationship between the LLP identified epidemiologic risk predictors and lung cancer. Inclusion of the SEZ6L SNP in the LLP risk prediction model improved calibration of the model and increased the area under the ROC curve by approximately 4%. Low, intermediate, and high risk thresholds were defined. Approximately 20-25% of predicted risks were reclassified in the combined model. The greatest benefit of the combined model was seen in the group with intermediate risk.

Comments

1. Our ability to accurately predict the risk of developing lung cancer will help advance lung cancer screening and prevention programs.
2. Several models have been developed that predict the risk of developing lung cancer using epidemiologic criteria.
3. This study has shown that risk prediction can be improved by combining epidemiologic with molecular predictors of risk.
4. Future work will optimize risk prediction using a combination of epidemiologic factors and biologic biomarkers.

SCREENING

Aberle DR, Adams AM, Berg CD, Clapp JD, Clingan KL, Gareen IF, Lynch DA, Marcus PM, Pinsky PF. **Baseline characteristics of participants in the randomized National Lung Screening Trial.** *J Natl Cancer Inst* 2010;102: 1771-9.

Summary
The National Lung Screening Trial (NLST) is a randomized controlled trial designed to determine if screening a group at high risk for developing lung cancer with computed tomography (CT) will reduce mortality from lung cancer relative to screening with a single view chest x-ray (CXR). 53,456 subjects, aged 55-74 with a history of at least 30 pack-years of smoking were recruited to one of 33 screening sites across the US from September 2002 through April 2004. Study subjects were imaged in their randomized group at baseline and yearly for 2 subsequent years. They were followed for a minimum of 5 years. Randomization was stratified by site, sex, and 5-year age group. Self-reported data about demographics and medical history were recorded. The composition of the NLST participants was compared to the general population at risk for lung cancer. 59% of the study population were men, the mean age was 61.4 years, 91% were white, 52% were former smokers, and the median pack-years of smoking was 48. Age, sex, ethnicity, education, marital status, smoking characteristics, occupational exposure, comorbidities, and family history were similar between the two arms. NLST subjects were younger, less likely to be current smokers, and were better educated than the general population at risk for lung cancer.

Comments

1. The presence and magnitude of known risk factors for lung cancer were equally distributed between the study arms suggesting the randomization procedure was effective.
2. NLST subjects were slightly younger, less likely to be current smokers, and were better educated than the general population at risk, but otherwise the sample studied seems to represent the general at risk population well.
3. In November, 2010, the NCI announced that there was a 20.3% reduction in lung cancer related mortality in the CT screening arm.
4. We look forward to future reports from the NLST describing some of the screening related issues that have been debated to date – false positives, procedures for benign nodules, radiation exposure, and cost effectiveness.
5. There is sure to be debate about the best way to translate the NLST study design and results into clinical lung cancer screening programs.

STAGING

Annema JT, van Meerbeeck JP, Rintoul RC, Dooms C, Deschepper E, Dekkers OM, De Leyn P, Braun J, Carroll NR, Praet M, et al. **Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: A randomized trial.** *JAMA* 2010;304: 2245-52.

Summary

Undetected mediastinal metastases can lead to unnecessary thoracotomies. This randomized study of surgical mediastinal staging alone vs. combined endosonography (EUS and EBUS) followed by surgical staging, sought to determine if the upfront use of endosonography could improve the detection of nodal metastases and reduce the rate of unnecessary thoracotomies. Patients with potentially resectable non-small cell lung cancer who had an indication for mediastinal nodal sampling were randomly assigned to one of the two staging arms. Endosonography was performed under moderate sedation with EUS followed by EBUS. Surgical staging was performed by mediastinoscopy. Systemic lymph node dissections performed if the patient went on to thoracotomy (negative mediastinal staging) were the reference standard in both groups. 241 patients were randomized between the two arms. The sensitivity for mediastinal nodal involvement in the surgery alone arm was 79% and for the endosonography plus surgical staging arm was 94% (p=0.02). The number of potentially avoidable thoracotomies in the surgery alone arm was 21 (18%) vs. 9 (7%) in the endosonography arm (p=0.02). There was no difference in the complication rates. All but one of the complications in the endosonography arm were related to a surgical staging procedure being performed.

Comments

1. Mediastinal nodal staging with combined EUS/EBUS endosonography followed by mediastinoscopy improved the detection of nodal metastases and reduced the number of avoidable thoracotomies when compared to mediastinoscopy alone.
2. A description of the relative impact of EUS and EBUS was not provided, nor was the time taken to perform the combined procedure.
3. Though moderate sedation was used for endosonography in this study, many find general anesthesia is necessary for thorough staging.
4. In the era of molecular testing, insuring adequate tissue is obtained for tumor characterization during mediastinal staging is another outcome to consider.
5. This study was performed at tertiary centers with the technology, skills, experience, and infrastructure required for all methods of mediastinal staging.

MOLECULAR CHARACTERIZATION

Zhu C, King K, Strumpf D, Weir BA, Meyerson M, Pennell N, Thomas RK, Naoki K, Ladd-Acosta C, Liu N, et al. **Prognostic and predictive gene signature for adjuvant chemotherapy in resected non-small-cell lung cancer.** *J Clin Oncol* 2010;28: 4417-24.

Summary

Meta-analyses suggest a benefit from adjuvant cisplatin-based chemotherapy (ACT) in stages II-IIIA non-small cell lung cancer, with no significant benefit noted in stage IB. Markers of prognosis and predictors of response to therapy may help select patients most likely to benefit from ACT. In this study, gene expression profiling was performed on samples from 133 subjects with stage IB and II non-small cell lung cancer enrolled in JBR.10, a randomized controlled trial of adjuvant vinorelbine/cisplatin versus observation (62 observed, 71 treated). A prognostic gene expression signature was developed from probe sets significantly associated with survival in the 62 observed subjects, then verified by RT-qPCR,

and finally tested in 4 independent microarray data sets. A 15 gene, stage independent, prognostic sig*Nature* was found to be capable of separating subjects into high and low risk groups (adjusted HR of 18 for lung cancer specific survival, $p < 0.001$; validation HRs 1.96 – 3.57 for overall survival). ACT significantly prolonged survival of high-risk patients (HR 0.33) but was not helpful to low risk patients (HR 3.67). Similar treatment benefits were noted in high risk groups with either stage IB or stage II.

Comments

1. This study identified a gene signature capable of both prognosticating for lung cancer outcome and predicting the benefit from ACT.
2. The gene signature was able to show the potential benefit of ACT even in high risk groups with stage IB non-small cell cancer.
3. We are moving into an era where characterization of lung cancer beyond histology and stage will help guide treatment decisions for our patients.
4. There were a large number of studies describing biomarkers capable of identifying and/or characterizing lung cancer published in 2010.
5. It will be interesting to see the results of studies evaluating the clinical impact of incorporating adequately validated biomarkers into diagnostic and treatment algorithms in the upcoming years.

TREATMENT

Kwak E, Band YJ, Camidge DR, Shaw AT, Solomon B, Maki RG, Ou SI, Dezube BJ, Janne PA, Costa DB, et al. Anaplastic lymphoma kinase inhibition in non-small-call lung cancer. *N Engl J Med* 2010;363: 1693-703.

Summary

EML4-ALK is an aberrant fusion gene occurring in 2-7% of non-small cell lung cancers. It encodes for a chimeric cytoplasmic protein with constitutive kinase activity. It most frequently occurs in relatively younger patients with minimal smoking histories, found to have adenocarcinoma of the lung. EML4-ALK fusion does not occur in tumors harboring EGFR mutations or MET amplification. The ALK protein is felt to drive the proliferation of the cancers in which it occurs. Crizotinib is an oral ATP-competitive selective inhibitor of the ALK and MET tyrosine kinases. In an open-label phase I trial of crizotinib for solid organ tumors, 2 subjects with non-small-cell lung cancer with ALK rearrangement had an excellent response to treatment. This led to the enrollment of 82 patients (from 1,500 analyzed) with advanced stage lung cancer, each of whom were shown to have ALK positive disease on FISH testing of paraffin embedded tumor samples, and an ECOG performance status of 0-2. Most (94%) had received at least one previous therapy. In this group, the overall response rate to crizotinib was 57% and the probability of progression free survival at 6 months was 72%. Nausea, diarrhea, and visual disturbances were the most common side effects.

Comments

1. Non-small cell lung cancers with ALK rearrangements appear to be highly susceptible to treatment with the ALK kinase inhibitor crizotinib.
2. ALK inhibition as a targeted therapy for lung cancer has been developed at a rapid pace.
3. These results raise hope that other subgroups of lung cancer, capable of responding to targeted treatments, will be able to be defined by molecular analysis.
4. In a companion article, two secondary mutations in the kinase domain of EML4-ALK, conferring resistance to ALK inhibition, were described in the tumor of a patient who relapsed during treatment with an ALK inhibitor.

TREATMENT

Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, Dahlin CM, Blinderman CD, Jacobsen J, Pirl WF, et al. **Early palliative care for patients with metastatic non-small-cell lung cancer.** *N Engl J Med* 2010;363: 733-42.

Summary

Palliative care can improve the quality of care and reduce the use of medical services. This study evaluated the effect of early palliative care on quality of life, the use of medical services, and the quality of end of life care in patients with metastatic non-small cell lung cancer. 151 newly diagnosed patients were randomly assigned to an early palliative care arm or a standard care arm. Those in the early palliative care arm met with a palliative care team within 3 weeks of study entry and at least monthly afterwards. General guidelines for palliative care management were followed and documented in this group. Health related quality of life, mood, and measures of health care use were collected. The primary outcome was the change in the Trial Outcome Index (TOI) at 12 weeks. No significant between group differences were noted at

baseline. At 12 weeks there was a significant benefit to being in the early palliative care arm demonstrated by a higher TOI score (p=0.04). In addition, those in the early palliative care arm had less depression, less aggressive end-of-life care, higher documentation of resuscitation preferences, a great duration of hospice care, and longer survival (11.6 vs. 8.9 months, p=0.02).

Comments

1. Involving palliative care services early in the management of patients with metastatic non-small cell lung cancer can lead to improvement in their quality of life, and survival.
2. The improvement in patient oriented outcomes was accompanied by signs of improved quality of care, less aggressive end of life care, and an alteration of the use of health care services.
3. This study was performed at a single tertiary care site with specialized thoracic oncology and palliative care teams, limiting its generalizability, but not its message.

OTHER ARTICLES OF INTEREST

EPIDEMIOLOGY

Johansson M, Relton C, Ueland PM, Vollset SE, Midttun O, Nygard O, Slimani N, Boffetta P, Jenab M, Clavel-Chapelon F, et al. **Serum B vitamin levels and risk of lung cancer.** *JAMA* 2010;303: 2377-85.

Slatore CG, Chien JW, Au DH, Satia JA, White E. **Lung cancer and hormone replacement therapy: Association in the vitamins and lifestyle study.** *J Clin Oncol* 2010;28: 1540-6.

D'Amelio AM, Cassidy A, Asomaning K, Raji OY, Duffy SW, Field JK, Spitz MR, Christiani D, Etzel CJ. **Comparison of discriminatory power and accuracy of three lung cancer risk models.** *Br J Cancer* 2010;103: 423-9.

SCREENING

Croswell JM, Baker SG, Marcus PM, Clapp JD, Kramer BS. **Cumulative incidence of flase-positive test results in lung cancer screening: A randomized trial.** *Ann Intern Med* 2010;152: 505-12.

Byrne MM, Koru-Sengul T, Zhao W, Weissfeld JL, Roberts MS. **Healthcare use after screening for lung cancer.** *Cancer* 2010;116: 4793-9.

PATHOBIOLOGY

Liu X, Sempere LF, Ouyang H, Memoli VA, Andrew AS, Luo Y, Demidenko E, Korc M, Shi W, Preis M, et al. **MicroRNA-31 functions as an oncogenic microRNA in mouse and human lung cancer cells by repressing specific tumor suppressors.** *J Clin Invest* 2010;120: 1298-309.

Henneke I, Greschus S, Savai R, Korfei M, Markart P, Mahavadi P, Schermuly RT, Wygrecka M, Sturzebecher J, Seeger W, et al. **Inhibition of urokinase activity reduces primary tumor growth and metastasis formation in a murine lung carcinoma model.** *Am J Respir Crit Care Med* 2010;181: 611-9.

STAGING

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MOLECULAR CHARACTERIZATION

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DIAGNOSIS

Herth FJ, Krasnik M, Kahn N, Eberhardt R, Ernst A. **Combined endoscopic-endobronchial ultrasound-guided fine-needle aspiration of mediastinal lymph nodes through a single bronchoscope in 150 patients with suspected lung cancer.** *Chest.* 2010 Oct;138(4):790-4

Summary
Endobronchial ultrasound (EBUS) and esophageal ultrasound (EUS) have emerged as valuable tools in the sampling of mediastinal and hilar lymph nodes and thus in the staging of lung cancer. Each modality alone reaches different lymph node stations but the combination of these modalities can reach almost all lymph nodes relevant to lung cancer staging. Traditionally, EBUS and EUS were performed separately and by different specialties. In this study, pulmonologists performed both EBUS and EUS in succession using a single EBUS scope. Sensitivity was 89% for EUS, 92% for EBUS, and 96% for the combined approach.

Comments

1. This study highlights the feasibility of performing a combined EBUS-EUS procedure by one operator using an EBUS scope.
2. The combined sensitivity of EBUS and EUS for the diagnosis and staging of lung cancer is very high and may be superior to mediastinoscopy.
3. This combined approach can overcome the logistical difficulties in scheduling different operators to do a combined procedure and reduce the cost of using multiple scopes.
4. Randomized clinical trials are needed to compare the yield of combined EBUS-EUS to that of mediastinoscopy.

TREATMENT

Sciurba FC, Ernst A, Herth FJ, Strange C, Criner GJ, Marquette CH, Kovitz KL, Chiacchierini RP, Goldin J, McLennan G; VENT Study Research Group. **A randomized study of endobronchial valves for advanced emphysema.** *N Engl J Med.* 2010 Sep 23;363(13):1233-44.

Summary
Bronchoscopic lung volume reduction is an evolving concept in the treatment of severe emphysema. Its goal is to mimic the benefits of surgical lung volume reduction in a less invasive fashion and in potentially sicker patients. In this study, the investigators randomized 220 patients to either receive endobronchial valves (EBV) or standard medical care (control group). At 6 months, the EBV group experienced an increase of 4.3 % in the FEV1 and 2.5 % in the distance traveled in the 6-minute walk test. However, the rate of complications by 12 months was 10.3% in the EBV group and 4.6% in the control group. The most common adverse events were COPD exacerbation, pneumonia, and hemoptysis. Greater benefits were seen in patients with radiographic evidence of heterogeneous emphysema and fissure completeness.

Comments

1. The FDA didn't grant approval for the valves used in this study due to concerns about the modest benefit and the high rate of adverse events.
2. Bronchoscopic lung volume reduction is likely to be beneficial in a selected patient population.

TREATMENT

Rahman NM, Maskell NA, Davies CW, Hedley EL, Nunn AJ, Gleeson FV, Davies RJ. **The relationship between chest tube size and clinical outcome in pleural infection.** *Chest.* 2010 Mar;137(3):536-43.

Summary
This study sought to determine whether small bore wire-guided *Chest* tubes perform as well as blunt dissection-inserted large bore *Chest* tubes in the management of pleural infection. This was a secondary analysis of a study designed to investigate the utility of fibrinolytic therapy in pleural infections. There was no significant difference in any study outcome among the different sizes of *Chest* tubes (outcomes included death, need for surgery, length of hospital stay, change in CXR, and lung function at 3 months). However, pain scores were significantly higher in patients receiving large bore *Chest* tubes.

Comments
1. Small bore chest tubes may perform equally to large bore chest tubes in the management of pleural infections. This challenges the classical teaching that larger chest tubes are needed to drain pleural infections and pus effectively.
2. Pain could be reduced significantly when using small bore chest tubes.

TRAINING

Wahidi MM, Silvestri GA, Coakley RD, Ferguson JS, Shepherd RW, Moses L, Conforti J, Que LG, Anstrom KJ, McGuire F, Colt H, Downie GH. **A prospective multicenter study of competency metrics and educational interventions in the learning of bronchoscopy among new pulmonary fellows.** *Chest.* 2010 May;137(5):1040-9.

Summary
This study's aim was to establish performance-based competency metrics for bronchoscopy among new pulmonary fellows, as well as to assess the effects of educational interventions on their bronchoscopy skill acquisitions. Pulmonary fellows' skills and knowledge were assessed using validated tools at pre-specified milestones. Two cohorts were studied: the first cohort received training in bronchoscopy as per the standards set by each institution, and the second cohort received educational interventions that included simulation bronchoscopy training and an online bronchoscopy curriculum. The study found significant variation in bronchoscopy skills among fellows at their 50th bronchoscopy. Simulation bronchoscopy training enhanced the speed of bronchoscopy skills acquisition.

Comments
1. This study emphasized that number-based competency in procedural training should be abandoned and substituted with performance-based assessment.
2. Simulation technology can speed procedural skill acquisition among trainees and reduce practice on patients.

OTHER ARTICLES OF INTEREST

DIAGNOSIS

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Ernst A, Simoff M, Ost D, Michaud G, Chandra D, Herth FJ. **A multicenter, prospective, advanced diagnostic bronchoscopy outcomes registry.** *Chest*. 2010 Jul;138(1):165-70.

Sterman DH, Recio A, Haas AR, Vachani A, Katz SI, Gillespie CT, Cheng G, Sun J, Moon E, Pereira L, Wang X, Heitjan DF, Litzky L, June CH, Vonderheide RH, Carroll RG, Albelda SM. **A phase I trial of repeated intrapleural adenoviral-mediated interferon-beta gene transfer for mesothelioma and metastatic pleural effusions.** *Mol Ther*. 2010 Apr;18(4):852-60.

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PEEP IN ALI/ARDS

Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, Slutsky AS, Pullenayegum E, Zhou Q, Cook D, Brochard L, Richard JC, Lamontagne F, Bhatnagar N, Stewart TE, Guyatt G. **Higher vs. Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome: Systematic Review and Meta-analysis.** *JAMA*. 2010; 303:865-73

Summary

In this individual patient data meta-analysis the authors combined results from 3 large randomized trials comparing higher versus lower levels of PEEP in patients with acute lung injury (ALI). The ALVEOLI, EXPRESS, and LOVS trials all compared different levels of PEEP while controlling tidal volumes and inspiratory pressures in all patients. A total 2299 patient were randomized in the 3 trials, with the higher and lower PEEP groups appearing similar at baseline.Overall adjusted mortality was not different between the 2 groups (RR 0.94; 95%CI 0.86-1.04). However higher PEEP appeared to have a different treatment effect in the presence or absence of ARDS ($PaO_2/FiO_2 < 200$; slightly over 80% of patients in both groups) with a p-value of 0.02 for interaction. The higher PEEP group also had less use of rescue therapies and death after rescue therapies. The authors conclude that higher vs. lower PEEP was not associated with improved hospital survival in all comers, but were associated with improved outcomes in patients with ARDS.

Comments

1. Studies have been trying to define the 'optimal PEEP' for more than 35 years; this meta-analysis represents a culmination of decades of research.
2. The overall results of this study suggest that a strategy of higher vs. lower PEEP in ALI/ARDS is safe and reduces need for rescue therapy.
3. Thinking about how PEEP could reduce mortality – by providing lung recruitment, increasing end-expiratory lung volume, reducing volutrauma and atelectrauma - it is logical that these effects would be most prominent in patients who have collapsed/decruited lung at baseline, i.e. those with more severe ARDS rather than mild ALI.
4. In patients with ARDS a strategy of higher PEEP appears a sound choice – the best method to determine exactly how high remains a subject for debate and investigation.

EARLY VS. LATE TRACHEOSTOMY

Terragni PP, Antonelli M, Fumagalli R, Faggiano C, Berardino M, Pallavicini FB, Miletto A, Mangione S, Sinardi AU, Pastorelli M, Vivaldi N, Pasetto A, Della Rocca G, Urbino R, Filippini C, Pagano E, Evangelista A, Ciccone G, Mascia L, Ranieri VM. **Early vs. Late Tracheotomy for Prevention of Pneumonia in Mechanically Ventilated Adult ICU Patients: A Randomized Controlled Trial.** *JAMA*. 2010; 303:1483-9.

Summary

In this randomized controlled trial investigators studied the influence of tracheostomy timing on ventilator-associated pneumonia (VAP). 600 patients ventilated for at least 24 hours with moderate SAPS II scores and multi-organ dysfunction scores of 5 or more were enrolled, and 419 were subsequently randomized 48 hours later when they had not significantly improved or worsened according to standardized criteria. They were randomized to receive percutaneous tracheostomy after 6 to 8 days (early group) or after 13 to 15 days (late group) of laryngeal intubation. In the early group 69% of patients actually received a tracheostomy, while only 57% of those in the late group received a tracheostomy. The primary endpoint was development of VAP; there was a statistically non-significant trend toward a reduction in VAP with early tracheostomy (14% vs. 21%; p=0.07). However, earlier tracheostomy was not associated with reductions in 28-day mortality, 1-year mortality, or length of hospital length of stay.The authors conclude that a strategy of early tracheostomy in mechanically ventilated patients did not reduce the incidence of ventilator-associated pneumonia.

Comments

1. Studies of early vs. late tracheostomy in mechanically ventilated patients are inherently challenging because of the difficulties in predicting early on, which patients will still be alive and receiving mechanical ventilation after 2 weeks.
2. This trial attempted to address this by using a 2-staged enrolment and randomization process, but still had a significant number in both groups (more in the late group) who did not need a tracheostomy.
3. Although ventilator-free days and ICU-free days were lower, without accompanying reductions in hospital length of stay and/or mortality, these findings are of questionable significance
4. These data suggest that in most patients early tracheostomy will not reduce VAP, shorten hospital stay, or lower mortality.

LUNG-PROTECTIVE VENTILATION FOR ORGAN DONORS

Mascia L, Pasero D, Slutsky AS, Arguis MJ, Berardino M, Grasso S, Munari M, Boifava S, Cornara G, Della Corte F, Vivaldi N, Malacarne P, Del Gaudio P, Livigni S, Zavala E, Filippini C, Martin EL, Donadio PP, Mastromauro I, Ranieri VM. **Effect of a Lung Protective Strategy for Organ Donors on Eligibility and Availability of Lungs for Transplantation: A Randomized Controlled Trial.** *JAMA*. 2010; 304:2620-7.

Summary

These investigators examined the effects of using lung-protective ventilation in brain-dead patients. Potential organ donors were randomly assigned to at least 6 hours of either a conventional or protective strategy: low tidal volume ventilation (6-8 ml/kg PBW), moderate PEEP (8-10 cm H2O), recruitment maneuvers after ventilator disconnects, and an apnea test performed on continuous positive airway pressure (CPAP). Conventional patients received tidal volumes of 10-12 ml/kg PBW, PEEP of 3-5 cm H2O, no recruitment maneuvers and an apnea test performed off the ventilator. At the end of the study intervention clinicians not involved in the study judged eligibility of lung for transplant, based largely on oxygenation status. A total of 118 patients were randomized (59 in each group) and they appeared well matched at baseline. There was a significantly higher proportion of lungs meeting eligibility criteria for harvest (the primary outcome) in the protective group (95% vs. 54%; p<0.001), and of lungs actually transplanted 54% vs. 27%; p=0.004). Serum increases in IL-6 and soluble TNF receptors were seen in the conventional but not protective group during the 6-hour study period. The authors conclude that use of lung-protective ventilation increased the number of eligible and harvested lungs in brain-dead patients.

Comments

1. The availability of organs for transplantation remains a rate-limiting step in the provision of transplant, particularly for lungs, where living-related donors are not possible.
2. This study importantly demonstrates that the way in which we manage the ventilator in potential organ donors can have a significant impact on organ availability.
3. Given the multi-faceted nature of the intervention, it is impossible to be certain which individual component was most important – however given the reliance on oxygenation criteria for determining organ suitability, it seems likely that the avoidance of derecruitment in the protective group may have averted the apparent deteriorations seen in many in the control group.

PEEP RESPONSE IN ARDS

Di Marco F. Devaquet J. Lyazidi A. Galia F. da Costa NP. Fumagalli R. Brochard L. **Positive end-expiratory pressure-induced functional recruitment in patients with acute respiratory distress syndrome.** *Critical Care* Med 2010;38:127-32.

Summary

In this physiological randomized crossover study the authors studied the degree functional lung recruitment in 16 patients with ALI/ARDS subjected to 2 different levels of PEEP. In addition to oxygenation and lung volume measurements, functional recruitment was measured by the lung diffusion for carbon monoxide (DLCO) using a rebreathing technique. 8 patients were responders (DLCO increase >20% from PEEP 5 to PEEP 15), while in the other 8 patients DLCO increased by <5% or decreased. Compared with non-responders, the responders had smaller lung volumes at lower PEEP, higher lower-inflection points on volume-pressure curves, and but similar baseline levels of PaO2/FiO2 and DLCO. End-expiratory lung volume increased in response to increased PEEP in both responders and non-responders, but in the non-responders this was accompanied by a decrease in the conductance of the alveolar membrane, resulting in no net change in DLCO. PaO2/FiO2 ratio increased numerically with higher PEEP in both groups, but this was

only statistically significant in the DLCO responders. The authors conclude that DLCO measurements give additional information about lung recruitment that is not always congruent with physical lung recruitment.

Comments

1. The interesting findings in this study is that despite improvements in end-expiratory lung volume being seen in almost all ALI/ARDS patients with increased PEEP, this recruited volume was physiologically active for gas exchange in only half of patients.
2. This finding implies that in some patients in whom we increase PEEP, the net result is an increase in lung overdistention rather than recruitment of functioning perfused alveoli.
3. While bedside measurement of DLCO may not be feasible in most ICUs currently, clinicians can use this information by being aware that some, but not all ALI/ARDS patients are likely to benefit from increased PEEP.
4. Functional recruitment is more likely in patients with more severe ARDS, and in those with a better oxygenation response and a reduction in arterial CO2 in response to increased PEEP

OTHER ARTICLES OF INTEREST

EPIDEMIOLOGY

Wunsch H. Linde-Zwirble WT. Angus DC. Hartman ME. Milbrandt EB. Kahn JM. **The epidemiology of mechanical ventilation use in the United States.** *Crit Care Med*2010; 38:1947-53.

Gajic O, Dabbagh O, Park PK, Adesanya A, Chang SY, Hou P, Anderson H 3rd, Hoth JJ, Mikkelsen ME, Gentile NT, Gong MN, Talmor D, Bajwa E, Watkins TR, Festic E, Yilmaz M, Iscimen R, Kaufman DA, Esper AM, Sadikot R, Douglas I, Sevransky J; and Michael Malinchoc; on behalf of the U.S. Critical Illness and Injury Trials Group: Lung Injury Prevention Study Investigators (USCIITG-LIPS). **Early identification of patients at risk of acute lung injury: evaluation of lung injury prediction score in a multicenter cohort study.** *Am J RespirCrit Care Med* 2011; 183:462-70

NOVEL MODES

Terzi N. Pelieu I. Guittet L. Ramakers M. Seguin A. Daubin C. Charbonneau P. duCheyron D. Lofaso F. **Neurally adjusted ventilatory assist in patients recovering spontaneous breathing after acute respiratory distress syndrome: physiological evaluation.** *Crit Care Med* 2010;38:1830-7.

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VENTILATOR-ASSOCIATED PNEUMONIA

Lacherade JC. De Jonghe B. Guezennec P. Debbat K. Hayon J. Monsel A. Fangio P. Appere de Vecchi C. Ramaut C. Outin H. Bastuji-Garin S. **Intermittent subglottic secretion drainage and ventilator-associated pneumonia: a multicenter trial.** *Am J Resp Crit Care Med* 2010;182:910-7.

VENTILATION FOR ARDS

Pipeling MR. Fan E. **Therapies for refractory hypoxemia in acute respiratory distress syndrome.** *JAMA* 2010;304:2521-7.

Sud S. Sud M. Friedrich JO. Meade MO. Ferguson ND. Wunsch H. Adhikari NK. **High frequency oscillation in patients with acute lung injury and acute respiratory distress syndrome (ARDS): systematic review and meta-analysis.** *BMJ* 2010;340:c2327.

Squadrone V, Massaia M, Bruno B, Marmont F, Falda M, Bagna C, Bertone S, Filippini C, Slutsky AS, Vitolo U, Boccadoro M, Ranieri VM. **Early CPAP prevents evolution of acute lung injury in patients with hematologic malignancy.** *Intensive Care Med* 2010;36:1666-74.

Sud S, Friedrich JO, Taccone P, Polli F, Adhikari NK, Latini R, Pesenti A, Guérin C, Mancebo J, Curley MA, Fernandez R, Chan MC, Beuret P, Voggenreiter G, Sud M, Tognoni G, Gattinoni L. **Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis.** *Intensive Care Med* 2010; 36:585-99.

WEANING

Jackson JC. Girard TD. Gordon SM. Thompson JL. Shintani AK. Thomason JW. Pun BT. Canonico AE. Dunn JG. Bernard GR. Dittus RS. Ely EW. **Long-term cognitive and psychological outcomes in the awakening and breathing controlled trial.** *Am J Resp Crit Care Med* 2010;182:183-91.

Jaber S, Petrof BJ, Jung B, Chanques G, Berthet JP, Rabuel C, Bouyabrine H, Courouble P, Koechlin-Ramonatxo C, Sebbane M, Similowski T, Scheuermann V, Mebazaa A, Capdevila X, Mornet D, Mercier J, Lacampagne A, Philips A, Matecki S. **Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans.** *Am J Respir Crit Care Med* 2011;183:364-71.

Costa R, Navalesi P, Spinazzola G, Ferrone G, Pellegrini A, Cavaliere F, Proietti R, Antonelli M, Conti G. **Influence of ventilator settings on patient-ventilator synchrony during pressure support ventilation with different interfaces.** *Intensive Care Med* 2010;36:1363-70.

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NEUROMUSCULAR BLOCKERS IN ARDS

Papazian L, Forel J-M, Gacouin A, Penot-Ragon C, Perrin G, Loundou A, Jaber S, Arnal J-M et al. **Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome.** *N Engl J Med* 2010; 363: 1107-16.

Summary

The use of neuromuscular blockers in ARDS may improve oxygenation but may also promote muscle weakness .

In this multi-centre, double-blind, RCT, 340 patients with the onset of severe ARDS within the previous 48 hours were randomized to receive 48 hours of either cisatracurium besylate (178 patients) or placebo (162 patients). Severe ARDS was defined as a PaO2/FiO2 ratio of < 150 with PEEP of >/= 5 cm H2O with a Vt of 6 to 8 ml/kg. Primary outcome was proportion of patients who died either before hospital discharge or within 90 days after study enrolment adjusted for baseline P/F ratio, plateau pressure and SAPS II score. The Hazard ratio for death at 90 days in the cisatracurium group compared to the placebo group was 0.68 (95% CI 0.48 to 0.98; p=0.04). Mortality at 28 days was significantly lower in the cisatracurium group. No incremental muscle weakness was detected in the cisatracurium group compared to placebo at 28 days using the MRC scoring system for weakness.

Comments

1. These provocative data appear to be contrary to current convention as we shift to a more awake and mobile ICU culture to mitigate ICU acquired weakness and other morbidities of severe ARDS.
2. However, early paralytic use may mitigate patient-ventilator dyssynchrony and minimize the risk of volutrauma and barotrauma
3. Attenuation of the exuberant inflammatory response in the injured lung may further reduce the propagation of inflammatory mediators that promote organ dysfunction.
4. The MRC score at 28 days may not wholly reflect the extent of ICU acquired weakness and longer-term follow-up data would be helpful to understand the impact of this short-term paralytic use.

TREATMENT OF ARDS

Craig TR, Duffy MJ, Shyamsundar M, McDowell C, O'Kane C, Elborn JS, McAuley DF. **A Randomized Clinical Trial of Hydroxymethylglutaryl-CoA reductase Inhibition for Acute lung Injury (The HARP study)** *Am J Respir Crit Care Med* 2010 Sept 24 (Epub ahead of print)

Summary

There is no effective pharmacological treatment for acute lung injury. Statins have shown promise in vivo and in vitro in modifying underlying mechanisms that mediate lung inflammation. Sixty patients were randomized to 80 mg simvastatin or placebo until cessation of mechanical ventilation or up to 14 days in this single centre, randomized double-blind placebo controlled trial.

Main outcomes were measures of daily pulmonary and non-pulmonary organ function. By day 14, the simvastatin group had improvements in non-pulmonary organ dysfunction but there was no statistically significant difference in oxygenation, respiratory mechanics or ICU mortality. Simvastatin significantly reduced BAL IL-8 levels but plasma CRP were not significantly different.

There were no important adverse events reported from Simvastatin use.

Comments

1. High dose simvastatin treatment up to 14 days had an excellent safety profile.
2. Statins are associated with improvement in organ dysfunction in lung injured patients.

3. Reduction of BAL IL-8 levels suggests that there was important mitigation of the inflammatory response in the pulmonary compartment of statin treated patients
4. Only 20% of screened patients were already on a statin and this observation supports the feasibility of future trials of statins in patients with ALI/ARDS.
5. This phase 2 study was not powered to detect a difference in duration of ventilation or mortality, and further clinical trials powered for important clinical outcomes are necessary (eg. SAILS and Irish Critical Care Trials Group among others).

TREATMENT OF pH1N1 LUNG INJURY/ARDS

Martin-Loeches I, Lisboa T, Rhodes A, Moreno RP, Silva E, Sprung C, Chiche JD et al. **Use of early corticosteroid therapy on ICU admission in patients affected by severe panemic H1N1 v influenza A infection.** *Intensive Care Medicine* 2011 37(2): 272-83.

Summary
The role for early administration of corticosteroids in H1N1 associated lung injury/ARDS remains unclear.

This was a prospective observational multicentre study from June 2009-February 2010. Two hundred twenty patients were analyzed and 70% of patients required mechanical ventilation. Fifty-seven percent of patients received corticosteroid treatment on admission to the ICU. Cox regression analyses demonstrated that early use of corticosteroids was not significantly associated with mortality (HR 1.3 95% CI 0.7-2.4, p=0.4) but was associated with an important increase in the rate of HAP (OR 2.2, 95% CI 1.0-4.8, p<0.05)

A separate analysis of only those patients with ARDS yielded similar results.

Comments
1. Early administration of corticosteroids in pH1N1 associated lung injury/ARDS does not improve survival.
2. Steroid administration has been demonstrated to cause harm in the form of increased rates of HAP in these patients.
3. Those patients with more severe lung injury who meet ARDS criteria similarly do not benefit from steroid administration.
4. Similar findings have been noted in SARS with the addition of significant osteoporosis and osteonecrosis seen in the longer-term in those patients exposed to high dose corticosteroid treatment.

OUTCOMES AFTER ARDS

Herridge MS, Tansey CM, Matte A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, Kudlow P, Cook D, Slutsky AS, Cheung AM and the Canadian Critical Care Trials. **Functional Disability Five Years after Acute Respiratory Distress Syndrome.** *N Engl J Med* In Press 2011

Summary
There are few detailed in-person follow-up data on 5-year outcomes after ARDS.

One hundred and nine ARDS survivors were evaluated at 3, 6 and 12 months and 2, 3, 4 and 5 years after ICU discharge. At each visit, patients were interviewed and examined, underwent pulmonary function tests (PFTs), 6 Minute Walk Distance (6MWD), resting and exercise oximetry, chest imaging, quality of life evaluation and report of healthcare utilization.

At 5 years, patients had reduced 6MWD of 436 meters (76 % predicted) and reduced Physical Component Score (PCS) of the Short Form (SF)-36 of 41 (age- and sex-matched mean norm score 50). Younger patients had the steepest recovery trajectory in the PCS of the SF-36 when compared to older patients, but each group failed to return to its normal predicted physical function. Pulmonary function was normal to near normal with a mild reduction in diffusion capacity. A constellation of other physical and psychological problems developed or persisted in patients and family caregivers up to 5-years. Patients with more comorbidities incurred greater 5-year costs.

Comments
1. Exercise limitation, physical and psychological sequelae, decreased physical quality of life and increased costs and healthcare utilization are important legacies of surviving severe lung injury.
2. There is a need for risk stratification to understand how to tailor rehabilitation to individual need
3. Interventions need to consider family caregivers who also sustain important morbidity over time and whose outcomes modify patient outcomes.

4. The pathophysiology of ARDS-related weakness and brain dysfunction requires urgent study.

REHABILITATION FOR ALI/ARDS

Needham DM, Korupolu R, Zanni JM, Pradhan P, Colantuoni E, Palmer JB, Brower RG, Fan E. **Early Physical Medicine and Rehabilitation for Patients with Acute Respiratory Failure: A Quality Improvement Project.** *Arch Phys Med Rehabil* 2010; 91: 536-42.

Summary

Immobility plays an important role in the development of ICU acquired weakness.

This was a seven month prospective before/after quality improvement (QI) project in a 16 bed MICU in a single centre. Fifty-seven patients participated who were mechanically ventilated for 4 days or more and who were cognitively intact without neuromuscular disease before their critical illness. The investigators used a structured QI process and change in practice was fostered through the "4Es" approach: engage, educate, execute and evaluate. Outcomes included daily use and dose of benzodiazepine, and narcotics, daily sedation and delirium status and daily functional mobility measures. In comparison with the pre-QI period, there was a significant reduction in the proportion of patients on benzodiazepines and narcotics, fewer days spent on these medications and lower median doses when administered. This resulted in more alert patients with less delirium. Also, this intervention substantially increased the proportion of patients who received PT and/or OT therapy, increased the number of therapies per eligible patient and MICU day with a functional mobility level of sitting or greater.

Comments

1. This QI program is feasible, safe and cost effective.
2. Through this structured process, important patient centred and administrative outcomes were achieved: reduction in delirium and improved functional mobility and a decrease in ICU and hospital LOS.
3. The study is limited by its' before/after design, lack of blinding, single institution experience but it effectively demonstrates the benefits of this intervention.
4. As a multifaceted process, the unique contribution of each of its modalities remains obscure.
5. The QI program targeted those patients with the best rehabilitation potential so it remains unclear how these outcomes might be altered in those with significant baseline neurocognitive or functional disability before ICU admission.

OTHER ARTICLES OF INTEREST

TREATMENT OF ARDS

O'Neal HR, Koyama T, Koehler EA, Siew E, Curtis BR, Fremont RD, May AK, Bernard GR, Ware LB. **Prehospital statin and aspirin use and the prevalence of severe sepsis and acute lung injury/acute respiratory distress syndrome.** *Crit Care Med* 2011 Feb 17 (Epub ahead of print)

OUTCOMES AFTER ARDS

Hopkins RO, Key CW, Suchyta MR, Weaver LK, Orme JF. **Risk Factors for depression and anxiety in survivors of acute respiratory distress syndrome.** *Gen Hosp Psychiatry* 2010; 32 (2): 147-55.

ECMO FOR PH1N1 ASSOCIATED ARDS

Roch A, Lepaul-Ercole R, Grisoli D, Bessereau J, Brissy O, Castanier M, Dizier S, Forel JM, Guervilly C, Gariboldi V, Collart F, Michelet P, Perrin G, Charrel R, Papazian L. **Extracorporeal membrane oxygenation for severe influenza A (H1N1) acute respiratory distress syndrome: a prospective observational comparative study.** *Intensive Care Medicine* 2010 ; 36 (11): 1899-905.

Nair P, Davies AR, Beca J, Bellomo R, Ellwood D, Forrest P, Jackson A, Pye R, Seppelt I, Sullivan E, Webb S. **Extracorporeal membrane oxygenation for severe ARDS in pregnant and postpartum women during the 2009 H1N1 pandemic.** *Intensive Care Med* 2011 Feb 12 (Epub ahead of print).