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Abstracts' Service

Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials

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Context. As of 2005, the International Committee of Medical Journal Editors required investigators to register their trials prior to participant enrollment as a precondition for publishing the trial's findings in member journals.

Objective. To assess the proportion of registered trials with results recently published in journals with high impact factors; to compare the primary outcomes specified in trial registries with those reported in the published articles; and to determine whether primary outcome reporting blas favored significant outcomes.

Data Sources and Study Selection. MEDLINE via PubMed was searched for reports of randomised controlled trials (RCTs) in 3 medical areas (cardiology, rheumatology, and gastroenterology) indexed in 2008 in the 10 general medical journals and specially journals with the highest impact factors.

Data Extraction. For each included article, we obtained the trial registration information using a standardised data extraction form.

Results. Of the 323 included trials, 147 (45.5%) were adequately registered (ie, registered before the end of the trial, with the primary outcome clearly specified). Trial registration was lacking for 89 published reports (27.6%), 45 trials (13.9%) were registered after the completion of the study, 35 (10.8%) were registered with no or an unclear description of the primary outcome, 39 (12%) were registered with no or an unclear description of the primary outcome, and 3 (0.9%) were registered after the completion of the study and had an unclear description of the primary outcome. Among articles with trials adequately registered, 31% (46 of 147) showed some evidence of discrepancies between the outcome registered and the outcomes published. The influence of these discrepancies could be assessed in only half of them and in these statistically significant results were favored in 82.6% (19 of 23).

Conclusion. Comparison of the primary outcomes of RCTs registred with their subsequent publication indicated that selective outcome reporting is prevalent.

Life-Science Research Within US Academic Medical Centers

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Context. Besides the generic "basic" vs "applied" labels, little information is known about the types of life-science research conducted within academic medical centers (AMCs).

Objedive. To determine the relative proportion, characteristics, funding, and productivity of AMC faculty by the type of research they conduct.

Design. Mailed survey conducted in 2007 of 3080 life-science faculty at the 50 universities with medical schools that received the most funding from the National lnstitutes of Health in 2004. Response rate was 74%.

Setting and Participants. Research faculty affiliated with a medical school or teaching hospital, representing 77% of respondents (n=1663).

Main Outcome Measures. Type of research (basic, translational, clinical trials, health services research / clinical epidemiology, multimode, other), total funding, industry funding, publications, professional activities, patenting behavior, and industry relationships.

Results. Among AMC research faculty, 33.6% exclusively conducted basic science research as principal investigators compared with translational researchers (9.1 %), clinical trial investigators (7.1%), and health services researchers / clinical epidemiologists (9.0%). While principal investigators garnered a mean of $410 755 in total annual research funding, 22.1% of all AMC research faculty were unsponsored, a proportion that ranged from 11.5% for basic science researchers to 46.8% for health services researchers ($P < .001$). The average AMC faculty member received $33 417 in industrysponsored funding, with most of this money concentrated among clinical trial ($110 869) and multimode ($59 916) principal investigators. Translational (61.3%), clinical trial (67.3%), and multimode (70.9%) researchers were significantly more likely than basic

science researchers (41.9%) to report a relationship with industry and that these relationships contributed to their most important scientific work ($P < .05$ for all comparisons).

Conclusion. The research function of AMCs is active and diverse, incorporating a substantial proportion of faculty who are conducting research and publishing without sponsorship.

Application of the Revised Lung Cancer Staging System (IASLC Staging Project) to a Cancer Center Population

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Objective. The International Association for the Study of Lung Cancer (IASLC) proposed a revision to the Union Internationale Contre Ie Cancer (UICC-6) staging system for non-small cell lung cancer. The goal of our study was to compare these systems in patients undergoing surgery for non-small cell lung cancer to determine whether one system is superior in staging operable disease.

Methods. Pathologic stages in 1154 patients undergoing complete resection over a 9-year period were analyzed. Patients were assigned a stage based on both IASLC and UICC-6 systems. We tested for statistically meaningful differences between the two staging systems using the Wilcoxon signed rank test and the permutation test.

Results. The IASLC system is more effective than the UICC-6 system at ordering and differentiating patients ($P = .009$). Application of the IASLC system resulted in 202 (17.5%) patients being reassigned to a different stage ($P = .012$), with the most common shifts occurring from IB to IIA and IIIB to IIIA. The 5-year and median survivals of the IASLC IIIA patients including those shifted from the UlCC-6 IIIB were 37% and 35 months, respectively. Reclassifying UICC-6 IIIB to IASLC IIIA did not reduce survival for the newly characterized IIIA cohort.

Conclusions. Our data confirm that the proposed IASLC staging system is more effective at differentiating stage than the UICC-6 system. Reclassifying patients from UICC-6 IIIB to IASLC IIIA will shift some patients from a stage previously considered unresectable to a stage frequently offered surgical resection. Further study and validation of the IASLC system are warranted.

Extrapleural Pneumonectomy Followed by Intracavitary Intraoperative Hyperthermic Cisplatin with Pharmacologic Cytoprotection for Treatment of Malignant Pleural Mesothelioma: A Phase II Prospective Study

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Objective. We sought to prospectively determine the feasibility and safety of hyperthermic intraoperative intracavitary cisplatin perfusion immediately after extrapleural pneumonectomy in the treatment of malignant pleural mesothelioma.

Methods. Patients with malignant pleural mesothelioma who were surgical candidates underwent extrapleural pneumonectomy followed by hyperthermic intraoperative intracavitary cisplatin perfusion, consisting of a 1-hour lavage of the chest and abdomen with cisplatin (42°C) at 225 mg/m^2. Pharmacologic cytoprotection consisted of intra- venous sodium thiosulfate with or without amifostine. Morbidity and mortality were recorded prospectively.

Results. Ninety-six (79%) of 121 enrolled patients underwent extrapleural pneumonectomy of whom 92 (76%) received hyperthermic intraoperative intra-ca-

vitary cisplatin perfusion after extrapleural pneumonectomy. Fifty-three (58%) patients had epithelial tumors, and 39 (42%) had nonepithelial histology. Hospital mortality was 4.3%. Morbidity (grade 3 or 4, 49%) included atrial fibrillation in 22 (23.9%) patients, venous thrombosis in 12 (13%) patients, and laryngeal nerve dysfunction in 10 (11%) patients. Nine patients had renal toxicity, which was attributable to cisplatin in 8 of them. Among the 27 patients who also received amifostine (910 mg / m^2), 1 patient had grade 3 renal toxicity attributable to cisplatin. Recurrence of malignant pleural mesothelioma was documented in 47 (51%) patients, with ipsilateral recurrence in 17.4% of patients. The median survival of the 121 enrolled patients was 12.8 months.

Conclusions. Hyperthermic intraoperative intracavitary cisplatin perfusion following extrapleural pneumonectomy can be performed with acceptable morbidity and mortality. The use of amifostine in addition to sodium thiosulfate might reduce cisplatinassociated renal toxicity. Hyperthermic intraoperative intracavitary cisplatinperfusion following extrapleural pneumonectomy might enhance local control in the chest.

Pitfalls in Donor Lung Procurements: How Should the Procedure be Taught to Transplant Trainees?

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Objective. The current trend in lung transplantation has led to liberalized lung donor selection criteria and use of marginal donors, with a corresponding requirement for improved procurement techniques to obtain high-quality donor grafts. Few reports, however, have provided recommendations for successful lung procurement procedures.

Methods. We retrospectively studied 47 lung procurements performed by the University of Pittsburgh Medical Center team from January 2007 to December 2007. From those findings, we compared outcomes, as well as technical errors encountered, between procurements performed by trainees with limited transplant experience and by experienced transplant surgeons.

Results. Twenty-two of the procurements (47%) were performed by experienced transplant surgeons and 25 (53%) by supervised trainees. Patient characteristics and technical difficulties were comparable between the two groups. The trainees took more time to complete the procedure than did the experienced surgeons, although the difference was not significant. Furthermore, 21 of the cases performed by trainees (84%) had one or more technical errors in the sequential steps of the procurement, including inadequate placement of the perfusion cannula in the main pulmonary artery (60%), insufficient topical cooling (56 %), and inadequate timing of the start of pulmonary artery perfusion (44%).

Conclusion. Donor lung procurements performed by beginners with limited transplant experience included frequent technical errors with regard to adequate graft preservation, which may lead to serious complications after transplant. Sequential steps in lung procurement techniques and better understanding of organ preservation should be an integral part of a lung transplant training program.

A 62-Year-Old Woman With Skin Cancer Who Experienced Wrong-Site Surgery: Review of Medical Error

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After a life-threatening complication of an injection for neck pain several years ago, Ms W experienced a wrong-site surgery to remove a squamous cell lesion from her nose, followed by pain, distress, and shaken trust in clinicians. Her experience highlights the challenges of communicating with patients after errors. Harmful medical errors occur relatively frequently. Gaps exist between patients' expectations for disclosure and apology and physicians' ability to deliver disclosures well. This discrepancy reflects clinicians' fear of litigation, concern that disclosure might harm patients, and lack of confidence in disclosure skills. Many institutions are developing disclosure programs, and some are reporting success in coupling disclosures with early offers of compensation to patients. However, much has yet to be learned about effective disclosure strategies. Important future developments include increased emphasis on institutions' responsibility for disclosure, involving trainees and other team members in disclosure, and strengthening the relationship between disclosure and quality improvement.

Silver Nitrate Through Flexible Bronchoscope in the Treatment of Bronchopleural Fistulae

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Objective. Bronchopleural fistula is a severe complication after pneumonectomy or lobectomy. Local application of silver nitrate to seal bronchopleural fistula was reported once 25 years ago with considerable success but was never repeated. We aimed to develop and evaluate a concrete technique of applying silver nitrate through a flexible bronchoscope to treat bronchopleural fistulae in central airways.

Methods. Consecutive patients with small (≤5 mm) bronchopleural fistulae in proximal airways were included in the study. After measurement of bronchopleural fistula size through a flexible videobronchoscopy, a standard bronchoscope cytology bruh covered with silver nitrate was passed through the working channel of the scope and was rubbed against the fistula's orifice producing balanching and edema on the mucosa. This procedure was repeated until closure of the fistula's orifice (treatment success) or absence of any tissue response after 2 bronchoscopic sessions (treatment failure).

Results. Of 16 patients referred, 5 were excluded from treatment because of large (>5 mm) fistulae. Among the 11 treated patients (median fistula diameter 3 mm, range 2-5 mm), treatment failure was observed in 2 patients in whom treatment was attempted early (15 days postsurgery). In the remaining 9 patients, treatment success was achieved (81.8% success rate) after a median of 2.5 (range 1-10) applications of silver nitrate. After 11 (0.5-24) months of follow-up, no relapse was observed among successfully treated fistulae.

Conclusion. The local application of silver nitrate through a flexible bronchoscopic brush produced a burn and healing process on the mucosa of small bronchopleural fistulae of the central airways, leading to effective and lasting treatment in most cases.