JOURNAL CLUB SUMMARIES

What's hot that the other lot got

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WHOLE-BODY MRI AS AN ALTERNATIVE STAGING STRATEGY IN NON-SMALL CELL LUNG CANCER

Accurate and efficient diagnostic pathways are essential in non-small cell lung cancer (NSCLC) staging as site and spread of disease typically dictate therapeutic options. Taylor *et al* (*Lancet Respir Med* 2019;7:523) prospectively evaluated the diagnostic accuracy for metastatic disease of staging pathways based on whole-body MRI (WB-MRI), compared with standard multimodality pathway in cases of newly diagnosed, but potentially radically treatable NSCLC. The Streamline L trial was implemented in 16 UK centres which screened 976 patients, recruiting 353 with 187 completing the trial protocol. Participants underwent WB-MRI in addition to standard staging investigations. Radiologists blinded to patients' clinical history (other than suspected cancer diagnosis) and contemporaneous imaging reported on local tumour stage and distant metastases. The local multidisciplinary team made the first major treatment decision based on standard investigations. The WB-MRI was then reviewed as if it were the initial staging investigation: any additional investigations deemed necessary were performed or reviewed to stage disease and decide on treatment. Compared with a reference standard established from a multidisciplinary consensus panel there was no significant difference in sensitivity for metastatic disease (n=52; WB-MRI 50% (95% CI 37 to 63), standard 54% (41 to 67), difference −4% (−15 to 7), p=0.73). There was a 10% difference in agreement of N stage (WB-MRI 65% vs standard 75%). Time-to-staging was shorter in WB-MRI pathways (13 days (12 to 14) vs 19 days (17 to 21)) which also had lower mean patient costs (£317 (273 to 361) vs £620 (574 to 666)). As diagnostic accuracy was similar to standard pathways, significant time and cost savings may support preferential use of WB-MRI in staging, particularly if similar improvements can be made in treatment delivery.

FORCED EXPIRATORY VOLUME IN ONE SECOND TO FORCED VITAL CAPACITY RATIO <0.70 IS ADEQUATE TO PREDICT COPD HOSPITALISATION AND MORTALITY

The hallmark of COPD is the presence of airflow obstruction defined by spirometry as a forced expiratory volume in one second to forced vital capacity ratio (FEV_1:FVC) of <0.70. As this threshold is primarily based on expert opinion, Bhatt *et al* (*JAMA* 2019;321:2438) performed a retrospective analysis to determine the discriminative accuracy of FEV_1:FVC across a range of fixed thresholds (0.65–0.75) and the lower limit of normal (LLN) for predicting COPD-related hospitalisation and mortality. Spirometric and outcome data were obtained from four of nine multiethnic cohorts of the US population based National Heart, Lung, and Blood Institute Pooled Cohorts Study. Complete data were available for 77% of 24 207 participants at 15 years of follow-up; 46% were male and 63% ever smokers. There were 6261 (26%) participants who had an initial pre-bronchodilator FEV_1:FVC <0.70. FEV_1:FVC of 0.70 demonstrated sensitivity of 66% and specificity of 79% for COPD-related events; negative predictive value was 0.92 but positive predictive value was only 0.37. Optimal discrimination for occurrence of COPD-related events was provided by a fixed threshold of 0.71 (C statistic 0.696 (95% CI 0.688 to 0.703)) in the general population and 0.70 (C statistic 0.670 (95% CI 0.678 to 0.695)) in subgroup analysis of ever smokers. Both fixed thresholds were significantly more accurate that LNN thresholds. This large population-based study provides clinical evidence to support the use of a fixed FEV_1:FVC threshold of 0.70 to identify those at risk of adverse COPD-related outcomes.

SEVERITY OF OBSTRUCTIVE SLEEP APNOEA IS GREATLY REDUCED WITH ATOMOXETINE AND OXYBUTYNIN

Current treatments for obstructive sleep apnoea (OSA) are based on physical manipulation of the oropharynx and/or upper airway for example, mandibular advancement devices or continuous positive airway pressure: such strategies are often poorly tolerated. Previous studies demonstrated increased upper airway patency and activity of the genioglossus muscle in response to agents with noradrenergic and muscarinic properties. Based on this, Taranto-Montemurro *et al* (*AJRCCM* 2019;199:1267) performed a randomised, double-blinded crossover trial in 20 subjects with previously diagnosed OSA comparing 80 mg atomoxetine and 5 mg oxybutynin (ato-oxy) with placebo, each taken on a single night. Despite the previous OSA diagnosis, five participants had an apnoea-hypopnoea index (AHI) <10/hour with placebo. Mean reduction in AHI was 15.9/hour (7.3 to 35.3) or 63% (33 to 86%) with ato-oxy compared with placebo (p<0.001). Despite the reduction in AHI sleep architecture and subjective sleep quality were similar between arms. Ato-oxy was well tolerated with only mild reported side effects. A subgroup (n=9) demonstrated no significant difference with oxybutynin or atomoxetine alone compared with placebo. Although limited by small size and short treatment duration, this study demonstrates clinical proof-of-concept to support further investigation into pharmacological treatment of OSA.

BROAD-SPECTRUM ANTIBIOTICS MAY BE ASSOCIATED WITH INCREASED MORTALITY IN COMMUNITY-ONSET PNEUMONIA

The use of broad-spectrum antibiotics for example, vancomycin and tazocin in the treatment of community-onset pneumonia is rising without evidence of increasing prevalence of drug-resistant pathogens (DRPs; eg, *Methicillin-resistant Staphylococcus aureus*, *Pseudomonas aeruginosa*) nor improvement in patient outcomes. Webb *et al* (*Eur Respir J* 2019:DOI 10.1183/13993003.00057-2019) performed a retrospective observational cohort study of immunocompetent adults (>18 years) admitted from four emergency departments in Utah, USA, treated for pneumonia. The authors used an unweighted multivariable regression analysis controlling for differences in demographics and markers of clinical severity (including eCURB score, intubation status, PaO_2/FiO_2). Of 1995 patients, 39.7% received broad spectrum antibiotics within 12 hours of presentation. Although the incidence of DRP was higher in the patients receiving broad spectrum antibiotics (7% vs <1%) the magnitude of the 30-day mortality was significantly larger than would be accounted by this alone (OR 3.8, 95% CI 2.5 to 5.9; p<0.001). Healthcare costs, length of stay and rates of *C. difficile* infection were significantly increased in the broad-spectrum antibiotic group (p<0.05). However the reason for the increased mortality is unclear: in manual review of mortality cases (n=40) consequences of broad-spectrum antibiotic use including *C. difficile* infection and acute kidney injury were identified in only 17.5%. Therefore other factors, including unmeasured confounders, may have contributed to the higher mortality.

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