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Trainee Section

Journal Watch

P Cockrell

Journals were reviewed between January and April 2011. The journals reviewed include: American Journal of Medicine, Annals of Internal Medicine, Archives of Internal Medicine, British Medical Journal, Gut, Heart, Journal of Hospital Infection, Journal of the American Medical Association (JAMA), The Lancet, Lancet Neurology, New England Journal of Medicine and Thorax. The articles chosen are those which were felt to have particular relevance to Acute Physicians.

Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study

Olesen JB, et al. BMJ 2011 Feb 5;342:320

The aim of this study was to compare CHA2DS2-VASc against CHADS2 stratification scheme in the assessment of thromboembolic risk in those with AF. This large cohort study demonstrated that the CHA2DS2-VASc score significantly improved risk stratification when compared to the CHADS2 system. The difference between the scoring systems seemed most marked in the assessment of those at low risk (a score of 0). Age and diabetes were the risk factors carrying the largest hazard ratio. It would seem that a decision to use aspirin therapy alone for the reduction of stroke risk in AF would best be made utilising the CHA2DS2-VASc system.

A registry based cohort study of 75,538 patients admitted between 1997 and 2006 with non-valvular AF was conducted. CHADS2 and CHA2DS2-VASc systems were both used to risk stratify all patients into low, moderate or high risk of thromboembolism with the primary end point being hospital admission or death from thromboembolism. A score of 0 with the CHADS2 and CHA2DS2-VASc system related to a thromboembolism rate per 100 patient years of 1.67% (95% CI 1.47-1.89%) and 0.78% (95% CI 0.58-1.04%) respectively. Subgroup analysis of the individual risk factors comprising the CHADS2 stratification system revealed that age >=75y was associated with the highest hazard ratio of 3.52 (95% CI 3.05-4.07) compared to hypertension which equated to the lowest hazard ratio at 1.45 (95% CI 1.17-1.79). Diabetes was associated with the highest hazard ratio of 3.47 (95%CI 1.65-7.27) when the individual risk factors comprising the CHA2DS2-VASc system were analysed.

Apixaban in Patients with Atrial Fibrillation

Connolly SJ, et al. NEJM 2011 Mar 3;364(9):806-17

Apixaban (a competitive inhibitor of factor Xa) was an excellent replacement for aspirin in those considered unsuitable for Warfarin when treating AF. When compared to aspirin, much lower rates of embolic events were demonstrated in the apixaban group as well as a statistically significant decrease in the number of those hospitalised for cardiovascular causes. This benefit was achieved without any elevated rates of serious bleeding when compared to aspirin. Although factor Xa inhibitors have been shown to be at least as good in reducing stroke risk as warfarin, this trial illustrates apixaban's safety in those usually prescribed aspirin when considered unsuitable for warfarin.

In this double-blinded study, 5,599 patients were selected who were assessed (utilising the CHADS2 score) as being at high risk of stroke as well as being considered unsuitable for warfarin. These patients were either prescribed aspirin 81-324mg OD or apixaban 5mg BD. Primary outcome was considered as either stroke (ischaemic or haemorrhagic) or systemic embolism. There were 51 primary outcome events (1.6% per year) in the apixaban group compared with 113 (3.7% per year) in the aspirin group. For primary outcome events the hazard ratio for apixaban when compared to aspirin was 0.45 (95% CI 0.32-0.62; p<0.001). The risk for first hospitalisation relating to cardiovascular cause, when comparing apixaban and aspirin groups, was 12.6% per year vs. 15.6% per year (p<0.001) respectively. The trial was

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terminated prematurely due to clear treatment benefit of apixaban following the first planned interim analysis of efficacy.

Clinical and economic impact of contaminated blood cultures within the hospital setting

Alahmadi Y M, et al. Journal of Hospital Infection 2011 Mar;77(3):233-6

Performed in a medium sized UK teaching hospital, this study illustrates the impact for the patient and hospital of false positive blood cultures. When matched for age and comorbidity a false positive blood culture resulted in an increase in hospital stay of 5.4 days and extra hospital cost of £5,001.50 per patient. With acute medicine frequently at the front line in the assessment of a potentially septic patient, the effect of minimising blood culture contamination should not be underestimated.

A retrospective case-control study was performed in a 426 bedded UK hospital. 142 false negative blood cultures from patients were matched to controls for age, comorbidity score (Charlson Index) and the month of admission to hospital. The increase in hospital stay and individual hospital costs related to the cases was 5.4 days (95% CI 2.8-8.1; p<0.001) and £5,001.50 (95% CI £3,283.90-£6,7190.1;p<0.001) compared to the controls. When scaled to the total number of false positive blood cultures for the whole hospital using the lower boundary of the 95% CI this amounted to a yearly cost of £834,111. Hotel rates for bed occupancy amounted for the vast majority of extra cost, but extra antibiotic therapy, laboratory and radiological tests did feature as a significant minority of extra expenditure.

Oral montelukast in acute asthma exacerbations: a randomised, double-blind, placebo-controlled trial

Ramsy C F, et al. Thorax. 2011 Jan;66(1):7-11

The beneficial bronchodilator effect of leukotriene receptor antagonists were studied in patients admitted with an acute exacerbation of asthma. A significant extra improvement in PEFR the morning after admission was shown in patients administered montelukast 10mg orally, in addition to receiving standard BTS therapy. Although the study was not large enough to prove a reduction in length of stay, the low side-effect profile of these medications alongside the early improvement in PEFR should encourage the use of montelukast in the acute setting.

A randomised, double-blind, placebo-controlled study compared the extra benefit of giving montelukast in addition to standard BTS advised therapy to those admitted with an acute exacerbation of asthma. The primary end point was the difference in PEFR improvement between the groups given montelukast or placebo, the morning after admission. The aim was to recruit 200 patients aged between 18 and 50, with an acute exacerbation of asthma displaying a PEFR of <=75% of best/predicted, in order to stand an 80% chance of showing a 25l/min difference at a 5% level of significance. The study was terminated early, with the analysis performed on only 73 patients, due to the slow rate of recruitment. The morning following admission the montelukast vs. placebo group had shown an extra improvement of 57.4l/min (95% CI 1.15 l/min - 113.6l /min).

The group receiving montelukast tended to have more severe asthma and tended to receive more magnesium and aminophyline. When reviewing these group differences with posthoc subgroup analysis, the positive montelukast effect was still present.

Risk of recurrence after venous thromboembolism in men and women: patient level meta-analysis

Douketis J, et al. BMJ. 2011 Mar;342:535

In patients presenting with their first unprovoked VTE, men were found to have a 2.2 fold higher risk of recurrence when compared to women. The rate of recurrence of VTE in women prescribed hormone therapy, once that therapy is discontinue, is low. When the hormone dependant female VTE group is excluded the rate of recurrence in men is still significantly higher (1.8 fold) than matched women. With this in mind clinicians may consider gender when deciding upon extended or lifelong anticoagulation in those with unprovoked VTE.

A meta-analysis of data from 2,554 individual patients derived from prospective studies was conducted resulting in the largest derived data source comparing recurrence rates of VTE in men and women.

Regression variables in the model were patient's age, cause of venous thromboembolism (unprovoked or provoked), hormone therapy, interaction between cause of venous thromboembolism and patient's sex, and extent of deep vein thrombosis (proximal or distal). The mean length of follow-up was 27.1 (SD 19.6) months. Incidence of recurrent VTE at 1 year for men and women was 9.5% (95% CI 7.9%-11.4%) and 5.3% (95%CI 4.1%-6.7%) respectively. The difference lengthens with time and by 5 years the incidence of recurrent VTE for men and women was 36.3% (95% CI 28.7%-45.9%) and 11.1% (95% CI 8.6%-14.4%) respectively.

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Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms

Zannad F, et al. NEJM 2011 Jan 6;364(1):11-21

Aldosterone antagonists are gaining ground in respect of the treatment of heart failure. The benefit of spironolactone in patients with NYHA III or IV has been well established (RALES) as well as eplerenone in heart failure following MI (EPHESUS). This study shows a significant reduction in rehospitalisation for heart failure and death from any cause in those treated with eplerenone when mild symptoms (NYHA II) are found in combination with a poor ejection fraction (<35%). Most of the patients joined the study within 6 months of being hospitalised for a cardiovascular cause. Acute physicians may want to advise general practitioners to consider starting eplerenone in patient's fulfilling these criteria following hospital admission.

2,737 patients aged >55y with an ejection fraction (in most cases) of no greater than 30% were recruited into this randomised, double-blind trial with a median follow-up of 21 months. Patients were prescribed either placebo or eplerenone 25mg OD increased to 50mg OD after 4 weeks (a reduced dosage regimen was used in those with an eGFR of 30-49ml/min). Primary outcome was death from cardiovascular causes or rehospitalisation for heart failure. The primary outcome occurred in 18.3% of the eplerenone group compared with 25.9% of the placebo group, giving a hazard ratio of 0.63 (95% CI 0.54-0.74; $p<0.001$). 12.5% of the eplerenone group died of cardiovascular causes compared to 15.5% of the placebo group, giving a hazard ratio of 0.76 (95% CI 0.61-0.94; $p=0.01$). Unsurprisingly, higher numbers of those in the eplerenone group suffered from hyperkalaemia.

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