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3.1 Should suspected patients with temporal arteritis (TA) have unilateral or bilateral temporal artery biopsy?,

TA is a patchy disease. Pathological findings in the temporal artery are distributed unevenly. Therefore discordance between left and right temporal; artery biopsies is possible.

173 consecutive cases of TA were biopsied. 132 of these underwent simultaneous bilateral biopsies. 51 had positive findings. 38 were bilateral positives and 13 only unilateral. If only unilateral biopsies had been performed in the 13 discordant cases, half the diagnosis (6 out of 51 = 13%) could have been missed.

Comment: Bilateral temporal artery biopsy can enhance diagnostic yield in suspected cases of TA. In several previous reports discordance between left and right biopsies ranged from 3-45%. The decision to perform bilateral biopsies simultaneously as an initial step or sequentially (with contralateral biopsy done only if the 1st biopsy is negative) can be individualized as in patients with unilateral tenderness or thickening of a temporal artery. The longer the biopsy segment the more likely a positive result will be obtained.

Ref: Breuer G.S. et al J. Rheumatol. 2009 Apr; 36: 794.

3.2 Is microalbuminuria (MA) a risk factor for venous thrombo embolism (VTE)?.

MA is a known risk factor for arterial thrombo embolic disease, and recent studies suggest that arterial and venous thrombo embolism have common risk factors. 8,574 adults (age range 28 – 75) in the Netherlands were followed up for 9 years. People with insulin dependent diabetes or pregnancy were excluded. There were 129 episodes of VTE. 50% were DVT and 50% pulmonary embolism. The annual VTE incidents rate was 0.12% in patients with normoalbuminuria vs 0.40% in those with MA. The hazard ratio was 2.0.

Comment: The clinical value of using MA as a marker for VTE risk is small as the absolute risk is very low. However the study suggest that MA is a marker for endothelial dysfunction in both arterial and venous systems. It also suggests a mechanism how statins interact with the endothelium to prevent VTE which has been recently reported (N.E.J. Med 2009; 360: 1851).

Ref: Mahmood B.K. et al JAMA 2009 May 6; 301 : 1790.

3.3 LDL cholesterol (LDLC) and highly sensitive CRP (hsCRP) lowering is beneficial for reducing cardiovascular events (CVEs).

In the JUPITER trials, healthy people with normal LDLC (< 130mg/dl) and elevated hsCRP (>2mg/l) who used Rosuvastatin 20mg daily had significant reductions in CVEs in 2 years of follow up. These findings suggest that anti inflammatory effect of statins make them useful for primary prevention even in subjects without hyperlipidaemia.

Now in a JUPITER sub study, 15,548 patients whose LDLC and hsCRP values were recorded 1 year after initiation with Rosuvastatin , it was found that there were largely independent reductions in both LDLC and hsCRP. Rosuva recipients whose LDLC remained > 70mg/dl had no significant reductions in adverse CVEs, whereas those who achieved this LDLC target had 55% fewer end points. hsCRP levels below 2mg/l led to significantly greater end point reductions than those

whose hsCRP levels remained above this value (RR 62% vs 31%). Patients who achieved both targets had better outcomes than those who achieved either one alone.

Comment: This analysis indicates that LDLC lowering below 70mg/dl and hsCRP levels below 2mg/l is useful in the primary prevention of cardiovascular disease. However the absolute reduction in end points in JUPITER was small (one event prevented per 100 patients treated for 2 years).

Ref: Ridker P.M. et al Lancet 2009 Apr 4; 373: 1175.

3.4 Is it possible to predict stroke in patients with asymptomatic carotid stenosis (ACS) ?.

In randomized trials, carotid endarterectomy (CE) for ACS, surgery lowered stroke risk by only a few % points in men and not at all in women.

A new international study of 821 patients (60% men and 40% women, median age 71) with ACS > 50% and no history of Ipsilateral stroke or TIA was undertaken. All underwent CT brain scan. CT findings suggestive of silent ischaemic events were classified as “embolic” or “non embolic”. During a mean follow up of 45 months, 6% experienced ipsilateral hemispheric strokes. In patients with 60 – 99% stenosis, annual stroke rates were significantly higher among those with silent embolic infarcts on baseline CT than among those without such infarcts (3.6% vs 1.0%).

Comment: Patients with ACS who choose surgery or stenting trade a small probability of immediate harm (perioperative stroke for a modest long term benefit). This study suggest that patients who already have CT evidence of silent embolic infarcts are most likely to benefit from surgery.

Ref: Kakkos S.K. et al J.Vasc. Surg. 2009 Apr; 49: 902.

3.5 Dipyridamole + Aspirin for haemodialysis graft patency .

For haemodialysis patients who have AV grafts, stenosis and thrombosis of the graft are important and costly complications. 649 haemodialysis patients with newly placed grafts were randomized to extended release dipyridamole + aspirin (Aggrenox) or placebo.

The incidence of the primary end point – graft patency without thrombosis or requirement for intervention – was significantly higher in the dipyridamole aspirin group than in the placebo group at one year (28% vs 23% ; P = 0.03). Graft patency was prolonged by an average of 6 weeks with the active drug.

Comment: In this study, aggrenox resulted in sdtatistically significant but quite modest prolongation of AV graft patency.

Ref: Dixon B.S. et al N.E.J.Med 2009 May 21; 360 : 2191.

3.6 Do antidepressants increase risk for diabetes ?.

A UK general practice research database looked at 2,243 adults who developed diabetes after starting antidepressant therapy compared with 8,963 sex and age matched patients who remained free of diabetes after a mean follow up of 2.8 years.

It was found that the diabetes risk was greater with SSRIs and tricyclics, when they were prescribed at or above median doses when use was recent (< 6 months before study entry) and long term (> 24 months). Long term treatment with paroxetine, fluvoxamine, venlafaxine and amitriptyline conferred elevated risk while fluoxetine, citalopram and sertraline long term use did not confer elevated risk. High BMI at base line was the strongest predictor for new onset diabetes.

Comment: Fluoxetine, citalopram and sertraline appear to be safe antidepressants for use in those predisposed to diabetes. Prior obesity is an independent risk factor.

Ref: Andersohn F et al Am.J.Psychiatry 2009 May; 166: 591.

3.7 PPIs and spontaneous bacterial peritonitis (SBP).

Proton pump Inhibitors (PPIs) have been recently shown to increase risk for several conditions such as pneumonia, Clostridium difficile infection and fractures. A lowered efficacy for concurrent clopedogrel has also been described.

In a recent retrospective case controlled study in patients with cirrhosis and ascites, SBP patients vs control patients had a much higher use of pre hospital PPIs (69 vs 31%). The odds ratio for increased risk after multivariate analysis of SBP with PPI use was 4.3. Half these patients were found to have no indications for the use of PPIs.

Comment: A proposed mechanism for the adverse effect of PPIs for SBP is the weakening of the acid barrier to GIT colonization by orally ingested bacteria. PPIs also abet bacterial over growth, translocation of bacteria across the intestinal wall, bacteraemia and seeding of ascetic fluid. Limiting the use of PPIs to valid indications make sense in all patients including those with cirrhosis and ascites.

Ref: Bajaj J.S. et al Am. J. Gastroenterol 2009 May ; 104: 1130.

3.8 Tamsulosin (T) and cataract surgery.

T is available in Sri Lanka as “Flomax” or “Urimax”. It is a strongly selective Alpha 1a blocker that relaxes smooth muscle in the prostate and the bladder neck. Because it also relaxes the iris muscle, it may lead to intra operative floppy iris syndrome (IFIS) and add to the difficulty of cataract surgery. Lost lens, lens fragment, retinal detachment and endophthalmitis were more likely complications when T had been used during the 14 days prior to surgery. T use prior to 14 days or use of other Alpha blockers such as terazosin and Doxazosin are not associated with increased complications.

Comment: Patients undergoing cataract surgery with prostatic or bladder problems should be advised to omit T at least 14 days before surgery and to replace it with another Alpha blocker.

Ref: Bell C.M. et al JAMA 2009 May 20 ; 301 : 1991.
Friedman A.H. IBID : 2044.

3.9 Folic acid for prevention of neural tube defects.

In 1996, the US Preventive Services Task Force (USPSTF) recommended folic acid supplementation for women of child bearing age (0.4 – 0.8 mg/d) for women who were planning pregnancy, starting one month before conception and through the first trimester and 0.4mg/d for all women capable of pregnancy. In 2009, the USPSTF update confirmed that folic acid supplementation resulted in fewer neural tube defects and was not associated with twinning, nor was there any potential harm of masking Vit B 12 deficiency.

The USPSTF now recommends that **all women who are planning or capable of pregnancy** take daily supplements containing folic acid **0.4 – 0.8 mg**. The supplementation should begin at least one month before conception and continue for 2-3 months afterwards. Higher doses might be beneficial for women with children who are affected by neural tube defects and for women who take certain anti seizure medicines like sodium valproate.

Ref: Ann.Intern.Med 2009 May 5; 150 : 626
Wolff T. et al IBID : 632.

3.10 TB as a cause of community acquired pneumonia (CAP).

Among drugs commonly used to treat CAP only the quinolones have excellent activity against Myc tb. Many instances of pulmonary TB mistakenly diagnosed as CAP have been treated with quinolones initially with short term improvement. The tuberculous cases improved temporarily with quinolones without quite resolving completely.

Comment: Clinicians should be alert to the red flag of CAP that seems to improve temporarily during quinolone treatment but yet never quite resolve.

Ref: Long R et al Clin .Infect. Dis 2009 May 15; 48 : 1354.

3.11 Serum - Ascites Albumin gradient (SAAG) in cirrhosis.

A SAAG of < 1.1 gm/dl normally implies an exudate such as in TB or peritoneal carcinomatosis and a level >1.1g/dl indicates a transudate. In cirrhosis however a SAAG of > 1.1g/dl was also seen in cirrhotic ascites complicated by TB, spontaneous bacterial peritonitis and peritoneal carcinomatosis. This is probably due to the fact that the exudate in these conditions is swamped by the transudative ascites of cirrhosis. Also in certain cirrhotic ascites there may be a gradient of < 1.1g/dl without any complicating exudative cause. This is evident when the ascitic fluid cell counts, cytology and cultures are negative.

Ref: Khandwalla H.E. et al Am.J.Gastro enterol 2009 Jun; 104: 1401.

3.12 Should ultrasound be used to determine the duration of anticoagulation after a DVT?

The optimal duration of anticoagulation after a DVT is not clear. Italian investigators randomized 538 patients with DVT who had completed 3 months of anticoagulation to either fixed or flexible continuation regimes. The fixed duration protocol involved 3 additional months of treatment for those with unprovoked DVT and none for those with secondary DVT. The flexible duration protocol involved additional 3 month courses until ultra sound venous Doppler showed recanalized veins (as long as 21 months for unprovoked DVT and 9 months for secondary DVT).

During 33 months of follow up, recurrent DVT or pulmonary embolism occurred in significantly fewer patients in the flexible duration group than in the fixed duration group (12 vs 17%). Incidence of major bleeding and death was somewhat higher in the flexible duration group.

Comment: Hitherto increased plasma FDP levels 2 weeks after withdrawal of anticoagulation was regarded as an indication to prolong the period of anticoagulation. Perhaps, ultrasound venous Doppler examination for absence of venous recanalization may be a complementary indication to prolong anticoagulation.

Ref: Prandoni P. et al Ann. Intern. Med. 2009 May 5; 150:577.

3.13 After carotid dissection which is better- Aspirin vs anticoagulation?.

Although uncommon, dissection of the extra cranial carotid artery accounts for a sizable proportion of strokes in younger patients. 298 consecutive patients with carotid dissection were reviewed. 2/3rd of the patients received heparin + warfarin and 1/3rd received aspirin alone. In this observational study, a negligible incidence of recurrent stroke with either treatment and a possibly higher risk for serious bleeding with heparin + warfarin – favour the use of aspirin after the carotid dissection.

Ref: Georgiadis D. et al Neurology 2009 May 26th ; 72:1810 and 1800.

3.14 PPIs vs H2 receptor blockers (HRBs) as a risk factor for hospital acquired pneumonia (HAP).

63,878 adult inpatients not in ICU were studied. 27,000 received PPIs and about 7,500 received HRBs. The incidence of HAP was 4.9% for all acid suppressant receivers and 2.0% who did not receive these drugs. The odds ratio (OR) for HAP who received acid suppressants was 1.3. The entire excess risk was attributable to PPI use. PPI use increased the risk for both aspiration and non aspiration pneumonias. The NNT to do harm with PPIs was 111.

Comment: The authors calculate that 0.9% of HAPs could be attributable to PPI use. Inappropriate PPI use in hospitalized patients should be avoided.

Ref: Herzig S.I. et al JAMA 2009 May 27; 301 : 2120.

3.15 Which is better to control dyslipidaemia - statins + niacin (N) or statins + ezetimibe (E)? (ARBITER 6)

The effect of N vs E when added to statin treatment was compared in a randomized open label blinded trial. All patients were already taking a statin and had LDLC < 100mg/dl, HDLC <55mg/dl

and coronary artery disease or a risk equivalent (diabetes or a 10year Framingham risk score of >20%). The primary endpoint was the change in carotid intima media thickness (CIMT) after 14 months. N=208.

The mean LDLC decreased by 18 mg/dl in the E group compared with 10mg/dl in the N group. N but not E was associated with a significant reduction in CIMT thickness. Also the rate of major CV events was higher in the E group than in the N group (5% vs 1%, P=0.04).

Comments: In this small trial, Niacin was superior to E in high risk patients on statin mono therapy. E usage is quite popular despite a lack of evidence that its ability to reduce the LDLC translate into patient benefits. The authors conclude that E should be a drug of last resort, if it is used at all.

Ref: Taylor AJ et. al. NEJ Med 2009 Nov 26; 361:2113

3.16 A new treatment for resistant hypertension – Endothelin receptor blockade (ERB).

Resistant hypertension(RH) is a BP remaining above the target level despite treatment with a diuretic and optimal doses of at least two other drugs. This is usually seen with older age, obesity, diabetes and chronic kidney disease.

Endothelin is a potent vasoconstrictor. Therefore ERBs would cause vasodilatation and lower BP. **Darusentan an ERB** was studied vs placebo in 379 RH patients at 117 International sites. Patients with heart failure or recent cardiovascular events were excluded. Target BP was achieved in 27% of placebo recipients and in 50% of Darusentan recipients. Oedema and fluid retention occurred in 27% of Darusentan recipients. These were treated with intensified diuretic therapy which cleared the oedema without substantial further decline in BP.

Comment: ERBs is a promising new strategy for treatment of RH, but risk for fluid retention would make it an unsafe choice for patients with heart failure. The drug has still not been FDA approved.

Ref: Weber M.A. et al Lancet 2009 Oct 24; 374: 1423.

3.17 What lipids should be measured to assess vascular risk?.

68 long term studies of lipids and cardiovascular disease involving about 300,000 patients with a mean follow up of 6 yrs was undertaken. TC, HDLC, TG, LDLC, non HDLC, Apo A1 and B were estimated and assessed. The risk for coronary artery disease was increased with high values of non HDLC, LDLC, non HDLC/ HDLC ratio , Apo B/A1 and lower values of HDLC. Risk for coronary artery disease and ischaemic stroke were not associated with TG levels. No difference in risk prediction was observed between fasting and non fasting measurements.

Comment: When direct measurements of LDLC is done without recourse to calculation from the TG level, and since cholesterol levels are not affected by fasting or non fasting – it may be appropriate and more convenient to estimate a lipid profile sans TG levels by a nonfasting estimation rather than a 12 – 14 hr fasting sample. Diabetics with mixed dyslipidaemia may still require a 12 hr fasting sample on initial and follow up examination. Those found to have only cholesterol elevation may not require fasting samples on subsequent estimations. TG levels unlike cholesterol require fasting samples.

Ref: Di Angelantonio E. et al JAMA 2009 Nov 11; 302: 1993.

3.18 B type natriuretic peptide (BNP) to rule out heart failure.

BNP levels are used to distinguish cardiac from non cardiac causes of dyspnoea. BNP levels can also be affected by age, BMI, atrial fibrillation (AF) and serum creatinine levels. The cut off values that produced a sensitivity of 91% in these subgroups (conventional threshold 100pg/ml) for the entire cohort were

Age over 75 = 184pg/ml.

AF = 150pg/ml.

S creatinine

(>2mg/dl) = 449pg/ml.

BMI

(>35) = 25pg/ml.

Comment: Age, BMI, AF and renal function are the most important patient characteristics to consider when using BNP levels to diagnose or rule out heart failure.

Ref: Rogers R.K. et al Am. J. Cardiol. 2009 Sept 1; 104:689.

3.19 H1N1 influenza – some aspects.

A Californian study looked at 1,088 PCR confirmed H1N1 infections between April and August 2009. Their findings were

1. Case rates were highest for infants (below 1 yr).
2. Lowest rates were for older adults (age over 70).
3. Fatality rates were considerably lower for hospitalized infants, children and teenagers.
4. Pneumonia was a common accompaniment in ICU admissions.
5. Severe disease occurred in diabetics, those with chronic lung disease or immunosuppressive disease.
6. Obese and morbidly obese diseased individuals were more prone to severe disease.

Ref: Louie J.K. et al JAMA 2009 Nov 4; 302: 1896.

3.20 MRSA – some aspects.

Recent MRSA infections which hitherto have been found to be Vancomycin sensitive are now being reported to be entirely or partially resistant to Vancomycin (VRSA). Linezolid and Daptomycin are newer agents. Some VRSA cultures have been found to be Methicillin susceptible. Such infections could be treated by a combination of Nafcillin, Rifampicin and Levofloxacin.

Comment: Staph aureus infection is usually treated with Flucloxacillin. If there are allergies or toxicities to penicillins, Vancomycin is the treatment of choice. If they are VRSA, then Linezolid or Daptomycin are alternatives. Just because an organism is methicillin susceptible, it doesn't mean that it is Vancomycin susceptible.

Ref: Pillai S.K. et al Clin. Infect. Dis. 2009 Oct 15; 49: 1169.

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