Vascular Society of Great Britain and Ireland

The following abstracts are from papers presented at the prize sessions to the 41st Annual Scientific Meeting of the Vascular Society of Great Britain and Ireland, held in Edinburgh, UK on 22–24th November 2006. The President of the Society, Mr John Wolfe was in the Chair. The BJS Prize was won by Mr MJ Bown, and the Founder's Prize was won by Mr GS McMahon. Both winners were from the University of Leicester, Leicester, UK. A complete list of the abstracts of papers presented at the meeting can be found on the BJS website (www.bjs.co.uk)

Smooth muscle cell proliferation is increased following percutaneous transluminal angioplasty – is combination antiplatelet therapy the answer?

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Objective: A limiting factor in the success of percutaneous transluminal angioplasty (PTA) is the development of restenosis secondary to smooth muscle cell (SMC) proliferation. This is mediated by activation of the mitogen-activated protein (MAP) kinase family including extracellular regulated kinase (ERK1/2). We hypothesised that SMC proliferation would increase in patients following PTA and that pre-treatment with clopidogrel could down-regulate this.
Method: A double-blind randomized controlled trial was conducted with 22 patients randomized to receive clopidogrel 75 mg or placebo for 30 days, in addition to their daily 75 mg aspirin. Loading was performed with 300 mg clopidogrel/placebo, at least 12 h before angioplasty. Plasma was sampled from patients at baseline, one hour before, and one hour, 24 h and 30 days after PTA. Twenty-four-hour growth-arrested rat vascular smooth muscle cells were incubated for 15 min with the plasma samples, and protein was subsequently extracted for Western blot analysis of ERK1/2 activation, as a surrogate marker of SMC proliferation.
Results: In 2/22 patients the baseline (pre-PTA) plasma maximally stimulated ERK1/2 activation. Of the remaining 20 patients, 19 had an increase in ERK1/2 activation post-PTA and only one showed no increase in activation. Overall, there was a 57% increase in ERK1/2 activation (s.d. 36) representing significant SMC stimulation ($P < 0{\cdot}001$). The observed effect on ERK1/2 occurred regardless of additional clopidogrel therapy ($n = 11$).
Conclusion: This is the first study to show that PTA significantly increases in vitro ERK1/2 activation. The use of combination antiplatelet therapy had no demonstrable effect in down-regulating the smooth muscle cell proliferation.

Penicillamine is a potent inhibitor of neointimal and medial thickening in porcine saphenous vein grafts

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Objective: Copper is an established risk factor for cardiovascular disease and atherogenesis, and has been shown to be elevated in patients with peripheral vascular disease and up to six weeks after coronary artery bypass grafting. It promotes oxidative stress, cell proliferation and matrix formation, all components of vein graft disease. We examined the effect of the copper chelator, penicillamine, on saphenous vein graft thickening.
Method: Saphenous vein into carotid artery interposition grafts were carried out in Landrace pigs. Penicillamine (10 mg/kg once daily; $n = 8$) was administered orally for one month and compared with controls ($n = 8$). Vein grafts were excised, fixed and histological sections prepared for morphometry and measurement of proliferating cell nuclear antigen (PCNA). Values are expressed as a median and 25th and 75th inter-quartile ranges. Significance was assessed using the Mann-Whitney U test.
Results: Administration of penicillamine had a significant inhibitory effect on neointimal thickness 0·14 (0·04–0·21) to 0·06 (0·04 to 0·09) mm ($P < 0{\cdot}01$), medial thickness 0·37 (0·29–0·41) to 0·23 (0·21–0·27) mm ($P < 0{\cdot}01$) and PCNA count 21·1 (19·9–23·0) to 12·5 (11·4–13·2) % ($P < 0{\cdot}01$). There was also a significant increase in luminal area 32 (25–37) to 50 (45–68) mm^2 ($P < 0{\cdot}01$) and a significant reduction in serum copper concentrations 12·6 (12·5–12·8) to 9·6 (9·3–10·2) μM/l ($P < 0{\cdot}01$).
Conclusion: The administration of penicillamine reduced vein graft thickening in this model. Copper chelators may be therapeutically useful in helping prevent late vein graft failure in patients undergoing reconstructive arterial surgery.

Antibiotic prophylaxis in varicose vein surgery: a double-blind randomized controlled clinical trial

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Objective: Wound infection rates of up to 13% have been reported following varicose vein surgery. The value of antibiotic prophylaxis in clean surgery is disputed. This double-blind randomized controlled clinical trial aimed to assess the value of antibiotic prophylaxis in patients undergoing saphenofemoral junction ligation, long saphenous vein stripping and phlebectomy.
Method: Patients undergoing groin surgery for varicose veins were randomized to receive co-amoxiclav 1·2 g intravenously ($n = 277$ limbs) or placebo ($n = 275$ limbs) on induction of anaesthesia. Patients completed a personal logbook over the initial 10-day postoperative period. Wound assessment was performed on days three, five, seven, nine and ten using a modified ASEPSIS score. Patients were reviewed at 14 days, and GP attendance, further antibiotic requirement, surgical intervention and need for readmission were determined.
Results: Groups were matched for demographics and wound infection risk factors. Postoperatively, patients receiving prophylaxis had: significantly lower ASEPSIS scores on days three, five and seven ($P < 0{\cdot}05$); lower global ASEPSIS scores ($P < 0{\cdot}05$ Chi-Squared test); fewer GP attendances (14·8 *versus* 30·6%, $P = 0{\cdot}0017$ Chi-squared test); reduced requirement for antibiotics (3·61 *versus* 9·49%, $P = 0{\cdot}0088$). Univariate and multivariate analyses demonstrated worse outcomes associated with: not receiving prophylactic antibiotics; a higher BMI; male sex. Age was associated with seeing a GP postoperatively, but not with a worse outcome.
Conclusion: Antibiotic prophylaxis significantly reduced wound-related problems following varicose vein surgery, and reduces the burden on primary care in the postoperative period.

Circulating interleukin-6: secretion by aortic aneurysms and the influence of aneurysm repair upon chronic levels

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Objective: Interleukin-6 (IL-6) plays a central role in the widespread inflammation that characterises abdominal aortic aneurysms (AAA). In addition, IL-6 has been identified as an independent risk factor for cardiovascular mortality. In vitro studies suggest that aneurysms secrete IL-6, which may be clinically relevant considering the majority of patients with aneurysms die from cardiovascular causes unrelated to aneurysm rupture. This study tested two hypotheses: (1) aneurysms secrete IL-6 into the circulation; (2) aneurysm repair reduces circulating IL-6 concentrations.
Method: (1) Prior to endovascular repair, blood was sampled from the entire length of the aorta in 27 patients with AAA and nine with thoracic aneurysms (TA). Fifteen patients undergoing angiography comprised controls. (2) Systemic venous blood was sampled in 99 patients with AAA and 100 outpatients that had previously undergone AAA repair. IL-6 was determined by ELISA.
Results: (1) Mean IL-6 concentrations were significantly higher in the aneurysm groups compared to controls (TA 10·36 pg/ml, AAA 4·94 pg/ml, controls 2·65 pg/ml; $P = 0·002$). Within the aneurysm groups IL-6 concentrations corresponded to aneurysm position, with significant differences throughout the aorta (AAA $P = 0·002$, TA $P = 0·008$, controls $P = 0·26$). (2) Systemic IL-6 levels were similar in the AAA and AAA-repaired groups (5·52 pg/ml *versus* 5·48 pg/ml; $P = 0·28$). However, circulating IL-6 was lower in patients that had undergone open repair compared to EVAR (4·2 pg/ml *versus* 5·9 pg/ml; $P = 0·03$).
Conclusion: These data support the hypothesis that aneurysms secrete IL-6 into the circulation, and suggest that the biological activity of AAA may continue despite endovascular exclusion. Both findings have implications for cardiovascular morbidity and mortality.

The IL-10 -1082 'A' allele and abdominal aortic aneurysm

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Objective: We have previously demonstrated that a single nucleotide polymorphism in the interleukin-10 promoter (IL-10 -1082) is associated with abdominal aortic aneurysm (AAA). The aim of this study was to confirm this finding in an adequately powered case-control study and explore whether this polymorphism was associated with AAA growth.
Method: This was a prospective case-control study of 390 patients with AAA and 404 screened controls without AAA; IL-10 -1082 genotypes, plasma IL-10 levels and AAA growth rates were recorded.
Results: There was a significant difference in IL-10 -1082 genotype ($P = 0·02$) and allele ($P = 0·006$) frequencies between the case and control groups. The IL-10 -1082 'A' allele was associated with an odds ratio of 1·327 ($P = 0·005$) for AAA and each additional 'A' allele was associated with an increase in odds ratio suggesting a co-dominant genetic effect. After controlling for age and gender these differences became more marked, the odds ratio for the 'A' allele as a risk for AAA being 1·835 ($P = 0·002$), again with an observed co-dominant genetic effect present. There was no significant difference in plasma IL-10 levels between the two groups and neither genotype nor allele positivity affected IL-10 levels. In the AAA group mean growth rate was 0·267 cm/yr, whilst there was a trend towards faster growth with the 'A' allele; this finding was not statistically significant.
Conclusion: This study confirms that the IL-10 -1082 'A' allele is associated with AAA and demonstrates that this genetic effect is co-dominant. This association is even stronger when age and gender are controlled for.

Dialysis-induced cerebral emboli (DICE): a pilot study

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Objective: Cerebral injury (CI), previously referred to as 'dialysis dementia', is frequent in haemodialysis (HD) and of unknown cause. We explored whether paradoxical cerebral embolization might be involved.
Method: One middle cerebral artery (MCA) and the return line subclavian vein were insonated by transcranial Doppler (TCD) for emboli throughout HD in 15 patients on long-term HD, six with cerebral injury (CI +ve) and nine without (CI −ve). Emboli were identified using international consensus criteria. Venous to arterial circulation shunts (v-aCS) were detected by a standardised TCD technique using a microbubble ultrasound contrast.
Results: There were no emboli in the return line subclavian vein prior to HD in any patient, but all had emboli at a mean of 9·3/min after 1 h and 15·6/min in the last hour of HD. Cerebral emboli were detected in four of the six (67%) CI +ve and none in the nine CI −ve patients. V-aCS were detected in three of the six (50%) CI +ve patients and in one of the nine (11·1%) CI −ve patients. All three CI +ve patients with a v-aCS also had cerebral emboli.
Conclusion: Emboli were infused intravenously throughout HD with some passing through a v-aCS to reach the brain. These results confirm the need for a case-control study powered adequately to test whether cerebral injury due to HD is associated with both v-aCS and cerebral emboli.

Low-molecular-weight heparin significantly reduces embolization after carotid endarterectomy: a randomized controlled trial

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Objective: Administration of heparin to patients undergoing carotid endarterectomy (CEA) transiently increases platelet aggregation, despite the use of aspirin. This may explain why some patients are more vulnerable to thrombo-embolic events in the early postoperative period. Since low-molecular-weight heparin (LMWH) is known to exert less effect on platelets than unfractionated heparin (UFH), we hypothesised this phenomenon would be reduced by using LMWH.
Method: One hundred and eighty-three patients taking aspirin who underwent CEA were randomized to 5000IU UFH ($n = 91$) or 2500IU LMWH ($n = 92$) prior to carotid clamping. Endpoints were: transcranial Doppler measurement of embolization, effect on bleeding (time from flow restoration to operation end) and, platelet aggregation to arachidonic acid (AA) and adenosine diphosphate (ADP).
Results: Patients randomized to UFH were twice as likely as those randomized to LMWH to experience a high number of emboli in the first three hours after CEA (odds ratio 2·06 (95% CI, 1·04–4·10), $P = 0·04$), which was not associated with increased bleeding (mean time from flow restoration to operation end was 23 min (UFH) *versus* 24 min (LMWH), $P = 0·18$). Platelet aggregation to AA significantly increased following systemic heparinisation, but there was no difference between heparin types ($P = 0·90$). However, the platelets of patients randomized to UFH exhibited significantly increased aggregation to ADP ($P < 0·0001$).
Conclusion: Intravenous LMWH (which is currently not licensed for use in CEA) is associated with a significant reduction in postoperative embolization (a recognised marker for increased risk of thrombosis) without increased bleeding. The enhanced UFH effect on embolization may be mediated by increased platelet aggregation to ADP.

Carotid intraplaque haemorrhage predicts recurrent symptoms in patients with high-grade carotid stenosis

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Objective: Although carotid endarterectomy has been shown to benefit patients with high-grade symptomatic carotid stenosis, a significant proportion will not have further events if treated on medical therapy alone. Carotid intraplaque haemorrhage (IPH) is a factor which has been associated with plaque instability. The aim of this study was to assess whether the identification of IPH by magnetic resonance plaque imaging predicts recurrent clinical cerebrovascular events.
Method: Sixty-six patients with a high-grade symptomatic carotid stenosis were prospectively followed until carotid endarterectomy or 30 days after MRI of the carotid arteries. The relationship between rate of recurrent ischaemic events and IPH was determined using a Cox regression analysis.

Results: Of the 66 patients who were followed up for a median of 21·5 days (interquartile range 9·0–43·3 days), 44 (66·7%) of their ipsilateral carotid arteries had IPH detected by MRI. Fourteen recurrent events were associated with IPH in the ipsilateral carotid artery, and only one amaurosis fugax occurred in the absence of IPH. IPH significantly decreased the event-free survival (log rank test= 6·9) with a hazard ratio of 8·0 (95% CI 1·1–60·9, $P < 0·05$) for recurrent ischaemic events.
Conclusion: IPH as detected by MRI predicts recurrent cerebrovascular events in patients with symptomatic high-grade carotid stenosis. A larger, multicentre study is warranted to establish whether the identification of IPH also predicts stroke alone, and to assess its added value in multi-factorial prediction models.

Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery

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Objective: This study investigated the volume-outcome relationship in surgery for abdominal aortic aneurysm (AAA) surgery and quantified critical volume thresholds for these procedures.
Method: PubMed, EMBASE and the Cochrane library were searched for articles on the relationship between hospital volume and mortality for AAA repairs. UK data were included by analysis of one year of the Hospital Episode Statistics (HES) database. Elective and ruptured AAA repairs were considered separately. The data were meta-analysed by comparing the odds ratios and 95% confidence intervals for mortality at higher- and lower-volume hospitals, along with the corresponding volume thresholds.
Results: Sixty-one articles were identified, in addition to the HES data, which provided 420,369 elective and 45,796 ruptured AAA cases. The mean mortality rates were 9·5% and 37·1%, respectively. The results provided conclusive evidence that higher-volume hospitals had reduced mortality for AAA repairs, especially for elective cases. The weighted cohort odds ratio was 0·66 (0·65–0·67) for elective repairs, with the critical operative volume threshold between higher and lower-volume hospitals identified as 40 repairs per annum. For ruptured AAA, the results were 0·78 (0·73–0·82) at a threshold of 15 repairs per annum. Values < 1 favoured surgery at higher-volume hospitals with smaller values holding a greater statistical significance.
Conclusion: Significantly lower mortality was associated with higher annual hospital volume of surgery for elective and ruptured AAA repair. These results suggested that AAA surgery should be performed only at higher-volume centres.

Surgery is superior to endovascular treatment of atherosclerotic renal artery stenosis (ARAS): a systematic review

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Objective: To investigate whether there is sufficient evidence to justify the current endovascular predominance in treatment of ARAS.
Method: Of 183 papers listed in PubMed, the USNLM and the Cochrane library (1975 and 2004), 58 dealing with outcomes of surgical and endovascular treatments (evidence levels IIb and III) were selected. Endovascular included 2788 patients in 21 prospective non-randomised (PNRT) and 13 retrospective (RET) studies. Surgical included 2857 patients in four PNRTs and 19 RETs. Demographic and outcome data were entered into SPSS®11 and subjected to regression analysis weighted according to the inverse variance method.
Results: Mean maximum surgical age was 79·39 (s.d.6·9) *versus* 83·61 (s.d.3·8) for endovascular treatment. Primary technical success was similar; however, endovascular patency declined at a monthly rate of 0·26% (95% CI 0·48–0·04%, $P = 0·03$). Significant findings in favour of surgery were: higher improvement for hypertension by 24% (95% CI 12–36%, $P < 0·001$) and for renal function by 37% (95% CI 24–50%, $P < 0·001$), greater decrease in mean systolic pressure by 18 mmHg (95% CI 8–28 mmHg, $P = 0·001$) and diastolic by 9 mmHg (95% CI 4–14 mmHg, $P = 0·002$) and higher mean creatinine reduction by 54 mmol/L (95% CI 28–80 mmol/L, $P < 0·001$). The low excess surgical mortality of 3·3% (95% CI 2·0–4·6%, $P < 0·001$) fell to an insignificant difference of 0·23% ($P = 0·63$) when concomitant aortic aneurysm repair was excluded.
Conclusion: These data question the overwhelming predominance of endovascular intervention in current treatment of ARAS and highlight the need for a carefully designed multicentre randomized controlled trial to identify which subset of patients would benefit more from surgical revascularisation.

The fate and clinical significance of tributaries at the saphenofemoral junction following endovenous laser ablation (EVLA) of the great saphenous vein (GSV)

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Objective: Although EVLA has been proposed for the treatment of varicose veins due to GSV reflux it is suggested that GSV tributaries at the saphenofemoral junction (SFJ) may remain patent, promoting persistent reflux and early recurrence of varicosities. This study assesses this concept.
Method: Fifty-one limbs (48 patients) were examined (duplex ultrasound) at a median of 12 months (IQR 10–12) after successful GSV ablation for primary varicose veins. SFJ reflux, tributary patency and varicose vein recurrence were recorded. Aberdeen Varicose Vein Severity Scores (AVVSS) were determined to assess the clinical significance of patent tributaries.
Results: No SFJ reflux was identified in any of the limbs, although at least one patent tributary was visible in 29/51 (57%) – group A. None demonstrated reflux. In 1/51 there was evidence of neovascularisation. In 21/51 (41%) limbs (group B) there was flush occlusion of the GSV with the SFJ and no detectable tributaries. There was no significant difference in AVVSS improvement between the groups: group A: pre-EVLA 13·8 (7·3–19·2), follow-up 2·9 (0·6–3·8); group B: pre-EVLA 14·9 (6·9–20·2), follow-up 3·1 (0·8–4·0). Recurrent varicosities were present in 1/51 due to an incompetent mid-thigh perforator.
Conclusion: EVLA results in flush occlusion of the SFJ, and no visible connection with GSV tributaries in 41% of patients. Even when tributaries did communicate with the SFJ no reflux was identified and no recurrent varicosities had developed as a result of this, suggesting that they are of no clinical significance up to one year after EVLA.

Stripping improves the results of short saphenous vein surgery at one year

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Objective: The aim was to examine the effect of various methods of short saphenous vein (SSV) surgery on outcomes.
Method: This was a prospective multicentre observational study involving 234 consecutive patients who had primary SSV surgery at one of nine UK NHS hospitals. Operative technique was determined by individual surgeon preference and clinical details, including the use of stripping, were recorded. One year after surgery, patients had venous duplex imaging and clinical assessment.
Results: A total of 204 patients were reviewed at one year. Some 67 had SSV stripping, 116 had saphenopopliteal junction (SPJ) disconnection only and the remainder had miscellaneous procedures. Clinical results: the incidence of visible residual varicosities at one year was lower after SSV stripping (14 of 67, 21%) than after disconnection only (35 of 116, 30%), although this did not reach statistical significance. There was no significant difference in the incidence of numbness at one year between those who had SSV stripping (14 of 67, 21%) and those who had disconnection only (29 of 116, 25%). Duplex results: the incidence of SPJ incompetence detected by duplex at one year was significantly lower in patients who underwent SSV stripping (9 of 67, 13%) than in those who did not (38 of 115, 33%) ($P < 0·01$).
Conclusion: Stripping of the SSV significantly reduced the rate of SPJ incompetence after one year without increased complications.