Vascular Society of Great Britain and Ireland

The following abstracts are from papers presented at the 45th annual scientific meeting of the Vascular Society of Great Britain and Ireland, held in Brighton 24–26 November 2010. The President of the Society, Professor Cliff Shearman, was in the Chair. The BJS Prize was won by J Chan, Vascular Surgery Unit, St Mary's Hospital, Imperial College Health Care NHS Trust London, and the Sol Cohen (Founder's) Prize was won by RE Clough of NIHR Comprehensive Biomedical Research Centre of Guy's and St Thomas' NHS Foundation Trust and King's College London, London.

Restenosis post-angioplasty is associated with increased smooth muscle cell proliferation in patients with intermittent claudication

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Objective: A limiting factor in the success of percutaneous transluminal angioplasty (PTA) is restenosis, presumed secondary to vascular smooth muscle cell (SMC) proliferation. We aimed to determine if patients who developed symptomatic restenosis 2 years post-PTA, expressed higher levels of SMC proliferation.

Method: Fifty claudicants undergoing PTA were randomised to receive blinded clopidogrel or placebo for 30 days in an ongoing trial. The relative ability of their plasma to stimulate extracellular regulated kinase (ERK)1/2 activation in a vascular SMC line in culture was measured at baseline, 1-hour pre-PTA, and 1-hour, 24-hours and 30-days post-PTA. Patients were followed for 2 years post-PTA, via clinics and retrospective case note review, to determine symptomatic restenosis.

Results: ERK1/2 activation was significantly increased 1-hour post-PTA irrespective of treatment with clopidogrel ($p = \cdot001$) or placebo ($p = \cdot013$). Three patients were excluded (technical failure, $n = 1$, abnormal baseline activation, $n = 2$). Nine patients required later re-intervention at the site of PTA for symptomatic restenosis. The plasma from these patients at 1-hour post-PTA produced a significantly ($p < 0{\cdot}05$) higher level of ERK1/2 activation in cultured SMCs (median 300%, range 246·5–537·5) compared to plasma from the 38 who did not require re-intervention (200%, 150–300). At later time-points there was no statistically significant difference.

Conclusion: SMC proliferation (represented by plasma ability to induce ERK1/2 activation in cultured SMCs) was significantly increased in patients developing a symptomatic restenosis post-PTA. This suggests a direct relationship between restenosis and the 'proliferative potential' of plasma, and likely reflects in vivo SMC proliferation. Further work is required to evaluate potential therapeutic treatments which may reduce peripheral PTA-induced SMC activation.

Activation of hypoxia-inducible factor (HIF) pathway in varicose veins

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Objective: Hypoxia has been postulated to contribute to varicose vein wall changes. Hypoxia-inducible factors (HIFs) are transcriptional factors that regulate the expression of genes of oxygen homoeostasis. The study aimed to compare HIF-1α, HIF-2α, and their target genes expression in varicose with non-varicose veins.

Method: Varicose and non-varicose veins were surgically retrieved from patients with and without varicosity, respectively. Protein and mRNA expression of HIF-1α, HIF-2α, and their target genes in varicose and non-varicose veins were analysed with immunoblot and real-time polymerase chain reaction. Data were presented as mean ± SEM, and analysed with an unpaired t-test and Mann-Whitney U test.

Results: HIF-1α and HIF-2α mRNA was up-regulated in varicose compared to non-varicose veins ($89{\cdot}8 \pm 18{\cdot}6$, $n = 11$ *versus* $10{\cdot}4 \pm 7{\cdot}2$, $n = 5$; $p = 0{\cdot}012$) and ($384{\cdot}9 \pm 209{\cdot}4$, $n = 11$ *versus* $8{\cdot}1 \pm 4{\cdot}2$, $n = 5$; $p = 0{\cdot}008$), respectively. Increased HIF-1α and HIF-2α protein expression was also observed in varicosities. The mRNA expression of HIF target genes was elevated in varicose compared to non-varicose veins; glucose transporter-1 ($8{\cdot}7 \pm 2{\cdot}1$, $n = 20$ *versus* $1{\cdot}0 \pm 0{\cdot}3$, $n = 10$; $p < 0{\cdot}001$), carbonic anhydrase-9 ($8{\cdot}5 \pm 2{\cdot}1$, $n = 20$ *versus* $2{\cdot}8 \pm 1{\cdot}2$, $n = 10$; $p = 0{\cdot}006$), vascular endothelial growth factor ($7{\cdot}5 \pm 2{\cdot}1$, $n = 20$ *versus* $0{\cdot}9 \pm 0{\cdot}2$, $n = 10$; $p = 0{\cdot}001$), BNIP-3 ($4{\cdot}5 \pm 0{\cdot}7$, $n = 20$ *versus* $1{\cdot}4 \pm 0{\cdot}3$, $n = 10$; $p = 0{\cdot}004$), enolase-1 ($11{\cdot}2 \pm 2{\cdot}1$, $n = 11$ *versus* $3{\cdot}1 \pm 1{\cdot}9$, $n = 5$; $p = 0{\cdot}019$), prolyl-hydroxylase domain (PHD)-2 ($5{\cdot}6 \pm 1{\cdot}1$, $n = 11$ *versus* $1{\cdot}7 \pm 0{\cdot}7$, $n = 5$; $p = 0{\cdot}034$), and PHD-3 ($9{\cdot}9 \pm 2{\cdot}2$, $n = 11$ *versus* $2{\cdot}4 \pm 1{\cdot}2$, $n = 5$; $p = 0{\cdot}047$). HIF target genes up-regulation in varicosities was also reflected at protein.

Conclusion: HIF-1α, HIF-2α, and target genes were up-regulated in varicose compared to non-varicose veins. Our data suggest the HIF pathway may be an important contributor to various structural and biochemical changes in varicosities.

Down-regulation of hypoxia-inducible factor 1α reduces venous thrombus resolution

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Objective: Hypoxia-inducible factor 1 (HIF-1)-mediated angiogenic factors are induced within venous thrombus during its resolution, but the primary stimulus for their production and thrombus resolution is unknown. Our aim was to determine whether down-regulating HIF-1α in the thrombus and vein wall reduces angiogenic factor expression, inflammatory cell infiltration, and thrombus resolution.

Method: Thrombus was induced in the inferior vena cava (IVC) of 40 mice. The mice were treated with the HIF-1α inhibitor, 2-methoxyestradiol (2ME, i/p, 150 mg/kg/day) or vehicle control ($n = 20$/group). HIF-1α, VEGF, and PLGF expression in the thrombus and IVC were measured at days 1 and 10 ($n = 7$/group) by enzyme-linked immunosorbent assay (ELISA). Thrombus size, neovascularisation, recanalisation, and macrophage and neutrophil infiltration were also measured at day 10 by image analysis ($n = 6$/group).

Results: The levels of HIF-1α ($p < 0{\cdot}001$), VEGF ($p < 0{\cdot}001$), and PLGF ($p < 0{\cdot}001$), and macrophage ($p < 0{\cdot}05$) and neutrophil ($p < 0{\cdot}005$) numbers were decreased in the thrombus of mice treated with 2ME compared with vehicle control. The levels of HIF-1α ($p < 0{\cdot}005$), VEGF ($p < 0{\cdot}005$), and PLGF ($p < 0{\cdot}001$), and macrophage ($p < 0{\cdot}005$) and neutrophil ($P < 0{\cdot}01$) infiltration were also decreased in the IVC wall surrounding the thrombus of 2ME-treated mice compared with controls. Thrombus neovascularisation ($p < 0{\cdot}005$) and vein recanalisation ($p < 0{\cdot}005$) were decreased, while thrombus size ($p < 0{\cdot}02$) and weight ($p < 0{\cdot}001$) were increased in 2ME-treated mice compared with controls.

Conclusion: Reducing HIF-1α expression in the thrombus and vein wall reduces angiogenic growth factor expression, inflammatory cell infiltration, and thrombus resolution. These data suggest that HIF-1α activity is an important regulatory mechanism in thrombus resolution.

The angiogenic potential of Tie2-expressing monocytes is impaired in patients with critical limb ischaemia

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Objective: Our pilot studies have shown that angiogenic monocytes (CD14+ve cells) expressing the angiopoietin receptor, Tie2, are mobilised in patients with critical limb ischaemia (CLI). We aimed to further investigate this angiogenic drive.

Method: The proportion of Tie2+ve monocytes was measured in blood from 40 patients with CLI, 20 age/sex-matched and 20 young controls by flow cytometry. A panel of 12 circulating angiogenic/inflammatory factors was measured by multiplex ELISA in CLI patients and controls (n = 10/group). An *in vitro* angiogenesis assay was used to compare lysates of Tie2+ve and Tie2−ve monocytes from patients and controls.

Results: Patients with CLI had 10-fold higher CD14+ve/Tie2+ve cells compared with age/sex-matched and young controls (3·52% ± 0·28 *versus* 0·39% ± 0·09 and 0·23% ± 0·04, respectively $p < 0·0001$). Tie2 expression was confirmed by RT-PCR. Circulating levels of angiopoietin-2 (799 ± 128 *versus* 384 ± 62 pg/ml), IL-6 (79 ± 29 *versus* 17 ± 6 pg/ml) and MCSF (39 ± 11 *versus* 14 ± 1 pg/ml) were significantly higher in CLI patients compared with controls, respectively ($p < 0·05$). Overall, Tie2+ve monocytes were more angiogenic compared with Tie2−ve monocytes (n = 18/group), inducing greater microtubule length ($p = 0·03$), tubule area ($p = 0·004$) and number of nodes ($p = 0·04$). However, the angiogenic potential of Tie2+ve monocytes from patients with CLI was lower than monocytes from healthy controls (n = 9/group), with reduced microtubule length ($p = 0·04$), tubule area ($p = 0·03$) and number of nodes ($p = 0·04$).

Conclusion: CLI is associated with a rise in Tie2+ve monocytes and the Tie2 receptor ligand, angiopoietin-2. This angiogenic drive may, however, be hampered by raised circulating levels of IL-6 and MCSF, which are systemic signals known to impair the angiogenic properties of monocytes.

Advancing what we know about genetics and varicose veins

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Objective: There is good circumstantial evidence which implicates genetics in the aetiology of varicose veins. The exact nature of the genetic basis remains unclear. The aim of this study was to consider the current reported genetic associations with varicose veins and to carry out a case control analysis to validate these using data from a genome wide association study (GWAS).

Method: An indirect, in silico, genome wide study of varicose veins was undertaken. This was based on our abdominal aortic aneurysm GWAS in which the frequency of varicose veins was similar in cases and controls. Genetic polymorphisms associations with venous disease to date were identified through a literature search. All known single nucleotide polymorphisms (SNPs), with > 5% allele frequency, in the genes previously implicated were analysed. Genotyping was carried out using Affymetrix Genome-Wide Human SNP Array 6·0.

Results: 349 patients with varicose veins and 857 controls were included. Genes which have been implicated in venous disease so far include FOXC2, HFE C282Y, Factor XIII V34L, oestrogen receptor B, TNF-A, MTHFR and thrombomodulin. None of the SNPs in these genes have shown significant association in this study. However, there were a number of other SNPs which were found to be associated with varicose veins and these are being validated in another cohort.

Conclusion: Previous candidate genes implicated in common venous disease have not been confirmed. A GWAS approach has been shown to be useful in validation and discovery of novel genes in venous disease but larger cohorts are required to confirm these.

The effect of novel texture features of homogeneity and echolucency on carotid plaque characterization; Results from the ACSRS study

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Objective: The effectiveness of novel ultrasound texture features - of both echolucency and homogeneity - on carotid plaque characterization, based on their risk for cerebral or retinal ischaemic (CORI) events was evaluated.

Method: An observational study was conducted in patients with 50–99% asymptomatic internal carotid artery stenosis. Baseline images from 1,121 patients from the Asymptomatic Internal Carotid Artery Stenosis and Risk of Stroke study were evaluated. Dedicated software provided us with 51 histogram/texture features of the plaque image. Factor analysis was used to identify redundant features. Hazard ratio analysis for CORI events was performed for the resulting features after adjustment for stenosis and after being controlled for established plaque factors (grey scale median, plaque area). Receiver operator curves (ROC) were used for model evaluation.

Results: A total of 130 ipsilateral CORI events occurred after a mean follow-up of 48 (range: 6–98) months. On survival analysis only the texture features Angular Second Moment of the Spatial Gray Level Dependence Matrices (SGLD_ASM) and the Run length distribution of the Gray level run length statistic (RUN_RLD) remained significant (HR: 3·3, 95% CI: 2·02 to 5·58, $p < 0·0001$ and 1·0, 95% CI: 1·01 to 1·04, $p < 0·0001$, respectively). Using ROC area under the curve, the new features improved the values of the established ones in distinguishing between the occurrence or not of CORI events (0·845 SE: 0·018, $p < 0·0001$ *versus* 0·80, SE: 0·019, $p < 0·0001$, respectively).

Conclusion: Carotid plaque echolucency and homogeneity can be simultaneously assessed by novel texture features. This may further improve the risk stratification of patients with asymptomatic carotid plaque disease.

Helix-B peptide of erythropoietin could be used as pharmacotherapy in critical limb ischaemia

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Objective: Pharmacotherapy has a limited role in the management of critical limb ischaemia (CLI). Erythropoietin (EPO), acting through its tissue-protective heteroreceptor complex (EPOR-CD131), is protective in many tissues and we have previously shown the expression and upregulation of EPOR-CD131 in ischaemic human skeletal muscle. However, EPO causes profound haemopoiesis, with increased risk of thromboembolism. ARA-290, a peptide that is derived from the helix-B of the EPO molecule, is tissue-protective but not haemopoietic. This makes it feasible for use in CLI. The aims of this study are to demonstrate the tissue-protective properties of EPO and ARA-290 in an *in vitro* model of skeletal muscle ischaemia and to assess the angiogenic potential of EPO and ARA-290 in vitro.

Method: An *in vitro* simulated model of skeletal muscle ischaemia was developed using skeletal myotubes cultured in hypoxic chambers. Myotubes were subjected to simulated ischaemia after pre-treatment with EPO or ARA-290. Apoptosis was measured by nuclear staining, cleaved caspase-3 assay and LDH release. Angiogenic potential of EPO and ARA-290 was assessed in human microvascular endothelial cells by proliferation, migration and capillary-like tube formation assays.

Results: ARA-290 and EPO significantly decreased the number of apoptotic nuclei, cleaved caspase-3 and LDH release in skeletal myotubes exposed to simulated ischaemia ($p < 0·01$). However, only EPO was found to significantly increase proliferation, migration and capillary-like tube formation of microvascular endothelial cells ($p < 0·05$).

Conclusion: ARA-290 may potentially reduce ischaemia-induced tissue damage in CLI whilst avoiding the side effects of EPO. The Results have provided us with a basis to conduct in vivo experiments.

Peak oxygen consumption is a useful biomarker in assessing survival after abdominal aortic aneurysm repair

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Objective: Abdominal aortic aneurysm (AAA) repair should be reserved for patients with a reasonable postoperative life expectancy. Exercise capacity is a more powerful predictor of mortality than established cardiovascular risk factors. The Objective of this study was to examine the association between performance on cardiopulmonary exercise testing (CPX) and 1-year survival in patients undergoing AAA repair.
Method: Between 2007 and 2009, 134 patients undergoing open or endovascular (EVAR) AAA repair underwent pre-operative CPX testing. Anaerobic threshold (AT) and peak oxygen consumption (VO_2 peak), expressed in ml kg^{-1} min^{-1}, were determined. Cardiovascular risk factors, 30-day and 12-month mortality were obtained from our database. The data were analysed for two groups, survivors and non-survivors; data are expressed as median (interquartile range).
Results: 134 patients (115 men) were studied; 70 open AAA repairs and 64 EVARs. Five patients died within 30 days (3·7%) and five within a year of surgery (1-year mortality of 7·5%). Groups were well matched for age and cardiovascular risk factors. Pre-operative VO_2 peak was significantly lower in non-survivors (15·3 [13·2–17·8] and 12·4 [9·3–16·5] in survivors and non-survivors, respectively, $p = 0·031$). AT was not different between the groups (10·7 [9·2–12·8] and 10·6 [8·4–12·5] in survivors and non-survivors, respectively, $p = 0·621$).
Conclusion: Median VO_2 peak was significantly less in patients who died within a year of AAA repair. This may provide a means of identifying patients who will not benefit from surgery. In contrast, AT is not an independent predictor of 1-year mortality, although this may reflect marked inter-observer variability in its derivation.

Integrin-α9-fibronectin interaction is required for normal murine venous valve morphogenesis

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Objective: Treatment of the complications of varicose veins and venous hypertension in the leg consumes >2% of the NHS budget. It remains unproven whether a primary defect in the venous wall or the venous valve (VV) initiates VV failure. We have shown that integrin-α9, encoded by Itga9 (identified in humans with congenital chylothorax) is expressed throughout the forming lymphatic valve (LV) and that binding to the EIIIA splice variant of fibronectin is required in LV formation. There are no data describing murine VV development. This study set out to describe VV morphogenesis, and examine VV phenotypes in mutant (Itga9 and EIIIA knockout) mice.
Method: Tie2-LacZ endothelial reporter mice combined with scanning electron microscopy (SEM) were used to characterise stages in normal murine VV development. Fluorescent-labelled antibodies to integrin-α9 and EIIIA were used with laser scanning confocal microscopy to examine expression patterns in developing VV in wild-type mice. SEM was used to phenotype VV structure in Itga9 and EIIIA heterozygous and homozygous knockout mice.
Results: Both Itga9 and EIIIA are expressed in VV leaflets, and homozygous knockout mice (for either gene; $n = 6$, $n = 2$ valves, respectively) display gross VV malformation or aplasia. Heterozygous knockouts had structurally normal VV.
Conclusion: This is the first description of murine venous valve morphogenesis and shows that there are genetic similarities (requirement for integrin-α9, fibronectin-EIIA) in the patterning of lymphatic and venous valves, which may reflect similar function. Characterisation of cell-extracellular matrix interactions in mice may provide insight into human VV disease.

Intra-plaque production of M1-type cytokines and matrix metalloproteinases differentiate stable from unstable carotid atherosclerosis

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Objective: Molecular and cellular characterisation of vulnerable atherosclerosis would help target functional imaging and plaque-stabilising therapeutics. We quantified cytokine and matrix metalloproteinase (MMP) protein production in symptomatic human carotid plaques to map the pro-inflammatory milieu responsible for plaque instability.
Method: Carotid endarterectomies from symptomatic ($n = 35$) and asymptomatic ($n = 32$) patients were enzymatically dissociated producing mixed macrophage-rich, atheroma cell suspensions which were cultured for 24 hours. Supernatants were interrogated with a 45-analyte panel on a Luminex 100 platform. Analyte inter-relationships were described statistically via Spearman correlation. Resulting sets were analyzed via Ingenuity Pathways Analysis v7·6. A 1·5-fold cut-off was set to identify proteins whose expression was significantly increased or decreased. Right-tailed Fisher's exact test determined significance (p-value) of protein over-representation compared to the result expected by a random protein set.
Results: Tumour necrosis factor (TNF)-alpha, interleukin (IL)-1alpha, IL-1beta, IL-6, IL-10, granulocyte-macrophage colony-stimulating factor (GM-CSF), macrophage colony-stimulating factor (M-CSF), CCL2, CCL5, CCL20, CXCL9, CXCL10, MMP1, MMP3, MMP8 and MMP9 levels were significantly higher in symptomatic than asymptomatic plaques ($p < 0·05$). A number of inter-related analyte 'clusters' were identified. Top-ranked biological pathways associated with differences between symptomatic and asymptomatic data sets (identified via Ingenuity) focused on the interplay between innate and adaptive immunity, nuclear factor-kappaB and MAPK signalling, hypercytokinaemia in inducing pathology and matrix degradation, and IL17 signalling.
Conclusion: The inflammatory milieu within human unstable plaque is in keeping with a predominance of M1-type macrophages with signatures of interferon-gamma and IL17 signalling. The novel finding in atherosclerosis of elevated CCL20 is further supportive of this Th17/IL17 signalling.

The potential therapeutic role of toll-like receptor 2 in critical limb ischaemia

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Objective: Inflammation and cell damage contribute to the pathophysiology of critical limb ischaemia. Toll-like receptors (TLRs) play an important role in inflammation and tissue damage possibly in response to endogenous ligands such as high mobility group box 1 (HMGB1). Functional TLR2 is expressed in skeletal muscle. We hypothesize that TLR2 signalling is upregulated resulting in an increase in the release of inflammatory cytokines such as interleukin-6 (IL-6) in muscle ischaemia.
Method: TLR2 expression was studied in ischaemic and control human muscle biopsies and *in vitro* using C2C12 myotubes cultured in simulated ischaemic conditions using Western blot. The functional effects of TLR2 antagonism on ischaemia-induced IL-6 release and cell death were studied by incubating myotubes with neutralizing TLR2 antibody. IL-6 release was assayed by ELISA. Apoptosis was assessed using cleaved caspase-3 and bax/bcl-2 ratio measurements. HMGB1 levels were measured using Western blot.

Results: TLR2 protein expression was significantly upregulated in critically ischaemic muscle and in C2C12 myotubes cultured in ischaemic conditions ($p < 0{\cdot}05$). IL-6 production increased in C2C12 myotubes cultured in simulated ischaemia. TLR2 antagonism reduced ischaemia-induced IL-6 production and apoptosis. Raised levels of HMGB1 were also demonstrated in the ischaemic C2C12 myotubes.
Conclusion: These Results show that TLR2 signalling is activated in ischaemic muscle leading to the release of cytokines such as IL-6 and contributing to inflammation and muscle damage. This could be activated by the endogenous ligand HMGB1. Further delineation of the TLR pathways may lead to strategies to reduce inflammatory damage in the treatment of critical limb ischaemia.

Clinical cell tracking of mononuclear cells using magnetic resonance imaging and superparamagnetic particles of iron oxide

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Objective: Cell therapy has emerged as a possible novel treatment option for critical limb ischaemia and following myocardial infarction. There is considerable interest in Methods for in vivo cell tracking to determine whether cells reach and remain in the target site. We have developed a protocol for labelling monocytes with superparamagnetic particles of iron oxide (SPIO), and evaluated its potential for use in human cell tracking studies.
Method: Up to 10^9 human mononuclear cells were labelled with SPIO. Labelling efficiency, viability and migration were assayed *in vitro*. Six healthy volunteers received intramuscular thigh injections of labelled cells, unlabelled cells and SPIO alone, and underwent T2-weighted (T2W) MRI. A phased-dosing protocol was used to assess the safety of intravenous infusion of labelled cells. Six further volunteers receiving $\sim 10^9$ SPIO-labelled cells underwent multiecho T2*W imaging of the liver and spleen before and after (2 hours–7 days) administration of cells.
Results: Efficient SPIO cell labelling was achieved without affecting *in vitro* viability or migratory capacity. SPIO-labelled cells were visualised on T2W imaging following IM administration. Intravenous administration of approximately 10^9 labelled cells was well tolerated and a significant reduction in $T2^*$ value was observed in the liver and spleen ($p < 0{\cdot}001$) reflecting accumulation of SPIO-labelled cells.
Conclusion: We have demonstrated for the first time in humans that SPIO-labelled mononuclear cells can be detected at a target site in a clinical MRI scanner following both local and systemic administration. This technique holds major promise as an important tool for the further development and monitoring of novel cell-based therapies.

Magnetic resonance T1 mapping predicts successful venous thrombolysis

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Objective: Novel thrombolytic delivery systems are changing the treatment paradigm for deep vein thrombosis (DVT), but older, well-organised thrombi remain unsuitable for intervention. A technique that identifies thrombi that are amenable to lysis is needed.
Method: An MRI 3D T1-mapping protocol was developed for imaging venous thrombi induced in mice. T1-relaxation times were quantified between 4 and 28 days after induction ($n = 33$). The thrombus was sectioned along its entire length. Collagen content was measured histologically as a marker of organisation and compared with T1-relaxation times in corresponding MR slices. Results were validated by three blinded observers. Tissue plasminogen activator (Actilyse) was injected (10 mg/kg) between 4 and 16 days after thrombus induction ($n = 16$). T1-mapping was performed before and 24 hours after Actilyse administration. Successful thrombolysis (vein recanalisation) was measured as an increase in the velocity of flow across the IVC greater than 0·3 cm/s (confirmed by histology).
Results: T1-relaxation time increases with thrombus age and organisation (763 ± 22 ms, 4d; 617 ± 36 ms, 7d; 673 ± 51 ms, 10d; 728 ± 58 ms, 14d; 945 ± 66 ms, 21d; 1194 ± 59 ms, 28d). Collagen content is proportional to T1-relaxation time during thrombus resolution ($R2 = 0{\cdot}80$, $p < 0{\cdot}0001$, $n = 15$). T1-relaxation times were significantly shorter in the group successfully treated with thrombolysis ($p = 0{\cdot}002$, $n = 16$). ROC curve analysis shows an optimal cut-off point of ~700 ms. The sensitivity and specificity for predicting successful thrombolysis was 100% and 88%.
Conclusion: This is the first study to show that T1-mapping quantifies organisation of experimental venous thrombi and predicts response to thrombolysis. This technique enables the Objective selection of thrombi that could be successfully treated with lysis in patients presenting with DVT.

Uptake of ultrasmall superparamagnetic particles of iron oxide predicts growth in abdominal aortic aneurysms

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Objective: In abdominal aortic aneurysm (AAA) disease focal hotspots of neovascularisation, inflammation and proteolysis represent areas at risk of expansion and rupture. Prediction of disease progression is challenging and currently relies on the simple measure of aneurysm diameter. We aimed to assess whether areas of cellular inflammation correlated with the rate of aneurysm expansion.
Method: Patients ($n = 29$; 27 male; aged 70 ± 5 years) with intact, asymptomatic AAA (4·0–6·6 cm) were recruited from a surveillance programme and underwent 3T MRI scanning before and 24–36 hours after administration of ultrasmall superparamagnetic particles of iron oxide (USPIO). The change in $T2^*$ value on $T2^*$-weighted imaging was used to detect accumulation of USPIO within the aneurysm. Aneurysm growth rate was determined using ultrasound. In patients undergoing open surgery, aortic wall tissue was obtained and stained for CD68 (macrophages) and iron (Prussian blue).
Results: Histological examination of aneurysm tissue confirmed uptake of USPIOs in areas of macrophage infiltration. Patients with distinct hotspots of USPIO uptake in the aneurysm wall ($n = 13$) had a three-fold higher growth rate (0·66 cm/yr; $p = 0{\cdot}020$) than those with no ($n = 7$; 0·22 cm/yr) or non-specific USPIO uptake ($n = 9$; 0·24 cm/yr), despite having similar aneurysm diameters ($5{\cdot}4 \pm 0{\cdot}6$, $5{\cdot}1 \pm 0{\cdot}5$ and $5{\cdot}0 \pm 0{\cdot}5$ cm, respectively; $p > 0{\cdot}05$). In one patient with an inflammatory aneurysm, widespread USPIO uptake extended beyond the aortic wall.
Conclusion: Uptake of USPIO in the aortic wall identifies cellular inflammation and appears to distinguish those patients with more rapidly progressive aneurysm expansion. This technique holds major promise as a new method of risk-stratifying patients with AAA.

The effect of n-3 long chain polyunsaturated fatty acid (n-3LCPUFA) supplementation on platelet and endothelial function in patients with peripheral arterial disease

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Objective: n-3 LCPUFA supplementation reduces platelet and endothelial activation in patients with or at risk of cardiac disease. We aimed to determine if n-3 LCPUFA supplementation in addition to best medical therapy can reduce the increased platelet and endothelial activity that is present in patients with intermittent claudication.

Method: 150 patients were recruited in a randomised cross-over double-blind study involving 6- week supplementation with OMACOR fish oil (850–882 mg eicosapentaenoic and docosahexaenoic acid) *versus* placebo. A 6-week washout period occurred between treatments. Patients with diabetes were excluded. For each outcome a mixed model analysis in which treatment, period and baseline values were fixed and patients were randomised was performed.

Results: Supplementation with omega-3 significantly reduced unstimulated p-selectin expression (−0·33 % expression [95% CI −0·64 to −0·03], p = 0·03). However, no effect was observed on other flow cytometry markers of platelet activation (stimulated p-selectin expression, stimulated/unstimulated fibrinogen binding) or platelet aggregation (ultegra point of care). Similarly, the markers of endothelial activation, pulse-wave velocity, S-ICAM and von-Willebrand Factor, along with the inflammatory markers C-reactive protein and IL-6, were also unchanged.

Conclusion: Supplementation with n-3 LCPUFA reduced unstimulated platelet p-selectin expression which has previously been shown to be elevated in patients with peripheral arterial disease and to increase with disease severity. It had no effect on markers of endothelial function.

Engineering a novel Ang1 mimetic for regenerative medicine applications

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Objective: In tissue engineering, improved vascularisation of the regenerated tissue is essential to overcome initial tissue mass loss. Angiopoietin 1(Ang1) is an angiogenic ligand essential for formation of functional blood vessels and with great potential for promoting tissue vascularisation. However, recombinant Ang1 is a large glycoprotein with variable solubility and biological activity and is difficult to produce. This study aims to develop small, stable Ang1 mimetic proteins for use as potential therapeutic lead molecules.

Method: Based on the mechanism by which the native ligand activates its receptor, a small synthetic ligand was designed. DNA sequences were constructed and expressed in E Coli. The synthetic ligand was isolated and purified and its ability to bind the angiopoietin receptor analysed by *in vitro* ELISA. Cell surface binding was examined by immunofluoresence staining and the ability of the ligand to activate cellular signalling was tested by phospho-specific immunoblotting. Functionally, the influence of the ligand on endothelial cell migration was studied using Boyden chamber chemotactic assay.

Results: A small synthetic ligand was produced. The ligand binds and activates angiopoietin receptors. In addition, it stimulates downstream signalling pathways including the phosphatidylinositol 3-kinase/Akt and Erk1/2 pathways. The ligand activates endothelial cell migration.

Conclusion: The novel synthetic ligands are easy to produce, highly soluble and stable, and activate the angiopoietin receptor. The properties of these synthetic ligands suggest they may be lead molecules for generating potential therapeutic Ang1 mimetics. In addition, the synthetic ligands can be immobilized on a tissue engineering scaffold to improve vascularisation of the engineered tissue.

Proteomic evidence of impaired resistance to oxidative stress and inflammation in the vasculature of patients with abdominal aortic aneurysms

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Objective: Proteomics may provide important insights into abdominal aortic aneurysm (AAA) pathogenesis. AAAs represent a systemic disease of the vasculature. AAA tissue demonstrates the end-stage of disease, limiting its utility in identification of factors initiating aneurysm development. Comparable morphological and molecular changes have been demonstrated in the vasculature of AAA patients distant from the aneurysm. Using a controlled comparative technique on vascular tissue from AAA patients, we sought to identify modified protein expression in the vasculature.

Method: Thirty-two patients, 16 with large AAAs and 16 matched controls were prospectively recruited. Inferior mesenteric vein (IMV) was harvested, homogenised and mined for differential protein expression. Difference in gel electrophoresis (DiGE), using a 2-D platform, identified protein spots with significantly altered intensity. MS/MS liquid chromatography characterized proteins of interest. DiGE findings were validated by Western Blotting (WB) and protein expression was localised within the IMV by immunohistochemistry (IHC).

Results: 1223 spots were demonstrated; 10 spots indicating clinically significant fold changes were explored further. 3/10 spots were identified: prohibitin (fold change [FC] × 1·9, p = ·002) and annexin A1 (FC × 1·6, p = ·002) were down-regulated in AAA patients; caspase-cleaved vimentin (FC × 1·5, p = ·04) demonstrated increased expression. All fold changes were confirmed by WB and localized to vascular smooth muscle cells (VSMCs) by IHC.

Conclusion: Proteins important in combating oxidative stress (prohibitin) and modulating inflammation (annexin A1) are reduced in the vasculature of AAA patients. There is evidence of increased apoptosis in VSMCs in these patients (cleaved vimentin). The proteomic changes demonstrated in this model of early aneurysmal disease may provide future therapeutic targets to combat AAA development.

Imaging of the vulnerable carotid plaque: biological targeting of inflammation using ultrasmall superparamagnetic particles of iron oxide (USPIO) and MRI

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Objective: Inflammation drives atherosclerotic plaque instability and acute thromboembolism, such as stroke. There is currently no clinical imaging technique available to assess the degree of inflammation associated with plaques. This study aims at visualising and characterising atherosclerosis using targeted USPIO as an MRI probe for detecting inflamed plaque disease.

Method: The initial *in vitro* feasibility study involved MRI detection of activated endothelial cells using anti-E-selectin antibody conjugated USPIO with confirmatory immunocytochemistry. In the ex vivo stage we have detected inflammatory markers on human atherosclerotic plaques harvested during carotid endarterectomy by anti-E-selectin antibody and anti-VCAM-1 antibody conjugated USPIO using MRI. In the in vivo stage we have detected atherosclerotic lesions in ApoE−/− mice using dual-targeted USPIO against VCAM-1 and E-selectin.

Results: We have established an *in vitro* model of endothelial cell inflammation, confirmed with both MRI and immunocytochemistry. We can now image inflammation of human atherosclerotic plaques by ex vivo MRI. The preliminary results showed that we are able to detect atherosclerotic lesions in ApoE−/− mice using dual-targeted USPIO against VCAM-1 and E-selectin.

Conclusion: We have successfully developed an *in vitro* model to detect and characterise inflamed endothelial cells by immunocytochemistry and MRI. We are able to image the degree of inflammation associated with atherosclerotic plaques by ex vivo MRI, and able to detect atherosclerosis in ApoE−/− mouse mice by in vivo MRI. This provides a new biologically-based imaging modality to identify the 'at risk' group with carotid plaque disease and aid decision making for appropriate intervention.

'Mini-sternotomy': a novel access for endografting of descending thoracic aortic aneurysms

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Objective: Endovascular thoracic aortic aneurysm repair is an alternative to the traditional open surgical repair. The endovascular approach is attractive by its potential to avoid the high morbidity and mortality associated with standard open surgical repair. The complexity of endovascular repair of thoracic aneurysms is increased by extensive atherosclerosis involving the aortoiliac segment. This study demonstrates the feasibility of endovascular repair of thoracic aortic aneurysms via a mini-sternotomy.
Method: From January 2002 through to October 2003, 7 patients underwent transluminal endovascular stent-graft placement for repair of thoracic aortic disease (one patient for thoracic aortic dissection while the remainder had descending thoracic aneurysms). Patients included in the study were those with extensive atherosclerosis and kinking involving the aortoiliac segment rendering the femoral access or iliac conduit not applicable or even hazardous. The follow-up protocol included early chest physiotherapy, a daily chest X-ray, U&Es, arterial blood gases and regular checks of distal pulsation till discharge. Patients underwent follow-up CT at 1, 6 and 12 months or at any occasion of suspected complications.
Results: No operative or postoperative complications were encountered during the in-hospital course of management of these patients, while during the 1-year follow-up we had one mortality 8 months following the procedure due to myocardial infarction.
Conclusion: The use of mini-sternotomy (manubriotomy) allowed excellent exposure of the aortic arch with visualization of the exact morphology of the proximal landing zone, so it can be used in patients with extensive atherosclerotic changes involving the aortoiliac segment where femoral access or iliac conduit is not feasible.

Medium-term outcomes of emergency EVAR for ruptured AAA

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Objective: Emergency endovascular aortic aneurysm repair (eEVAR) is rapidly becoming the treatment of choice for ruptured abdominal aortic aneurysms (rAAA) where facilities and expertise are available. Although studies have demonstrated that eEVAR is associated with reduced peri-operative mortality, relatively little is known about longer-term outcome following eEVAR. In particular, whether eEVAR confers a long-term survival benefit compared to open rAAA repair remains unknown. The aim of this study was to evaluate the medium-term outcomes of eEVAR for rAAA at our institution.
Method: A prospective database of all patients undergoing eEVAR from January 2006 to April 2010 for rAAA at our institution was analyzed.
Results: Fifty-two patients (45 male), median age 78 years (range 62–92 years), have undergone eEVAR for rAAA. The median length of stay was 11 days (IQR 7–25 days). There have been three (6%) late re-interventions (2 endovascular, 1 surgical). At a median follow-up of 25 months (range 2–52 months) there have been 15 deaths (29%), of which 6 were inpatient deaths (12%). Overall survival was 82% at 1 year and 73% at 2 years.
Conclusion: Emergency EVAR is associated with excellent medium-term survival in this cohort that included patients deemed unfit for open repair. We would recommend eEVAR to be the management of choice for rAAA in anatomically suitable patients where the local facilities and expertise exist.

The effect of mismatch between native anatomy of visceral aorta and design of fenestrated stent-grafts

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Objective: Accurate measurement of native anatomy is required to plan devices for fenestrated endovascular aneurysm repair (fEVAR). Measurements are subject to observer variability and potentially mismatch between the native anatomy and the stent-graft configuration. The aim of this study was to examine the effect of mismatch between fenestrated stent-grafts and native anatomy on proximal seal.
Method: A 36 mm proximal main-body incorporating two fenestrations and a scallop was deployed within a series of phantoms depicting visceral aorta. One phantom was produced with perfect alignment between the visceral vessels and fenestrations. Six additional phantoms were created with incremental mismatch in both the circumferential (n = 3) and longitudinal position of the renal vessels (n = 3). Qualitative assessment of apposition between the seal zone of the phantom and the stent-graft fabric was made by visual inspection and radiography. The degree of stent-graft distortion and misalignment of the scallop in relation to the superior mesenteric artery (SMA) as a result of stent-graft/phantom mismatch was also assessed.
Results: Fabric to lumen apposition (seal) was maintained in all phantoms. A circumferential discrepancy of 30° did not result in scallop misalignment. Partial SMA shuttering was observed at 45° and a discrepancy of 60° resulted in complete shuttering with partial shuttering of the renal arteries. Attempts to correct shuttering of the SMA with a balloon expandable stent resulted in partial crushing of the stent. In the longitudinal direction, discrepancies in vessel separation between −5 and 8 mm were tolerated without compromising target vessel patency.
Conclusion: Fenestrated stent-grafts appear to tolerate considerable mismatch with aortic anatomy without compromising seal. Additional factors such as the effect of mismatch upon deployment and durability of target-vessel stents merit further study.

Reducing the risk of spinal cord ischaemia following endovascular repair of thoracoabdominal aneurysms - the 'sac perfusion branch'

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Objective: Spinal cord ischaemia (SCI) is one of the most feared complications following repair of thoracoabdominal aneurysms (TAAA). The greatest risk is in the early postoperative period during episodes of cardiovascular instability. The aim of this study is to describe our early experience of a technique for maintaining perfusion of the intercostals and lumbar vessels in the early postoperative period following endovascular repair of Type II TAAA with branched stent-grafts.
Method: Patients underwent staged endovascular repair of TAAA. Perfusion of the intercostal vessels was maintained in the early postoperative period by a temporary controlled endoleak achieved with 'sac perfusion branches' added to custom-made stent-grafts. The repair was then completed 7–10 days later by percutaneous closure of the branches.
Results: There were five males and two females, mean age 74, with a mean aneurysm diameter of 6·8 cm. Standard precautions for the prevention of SCI were taken, including spinal drains. One patient developed monoparesis of the right leg during a period of hypotension secondary to a cardiac event and succumbed within 30 days. Of the remaining patients, there was no permanent paraplegia. One developed lower limb weakness following closure of the perfusion branches, with recovery following CSF drainage and revascularisation of the left subclavian. There have been no further complications or re-interventions.
Conclusion: Controlled perfusion of the intercostal vessels with a temporary controlled endoleak is feasible. Sac perfusion branches may be a useful adjunct to prevent SCI, providing protection to spinal cord perfusion during the immediate postoperative period, when the risk of cardiovascular instability is greatest.

Stent-graft limbs deployed into the external iliac artery are at increased risk of occlusion following EVAR

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Objective: Stent-graft limb occlusion is a common reason for re-intervention following endovascular aneurysm repair (EVAR). We assessed whether deployment of the endograft limb in the external iliac artery (EIA) increased the rate of limb occlusion.
Method: A prospectively maintained database of infra-renal EVAR procedures carried out in a single centre was analysed for stent-graft limb occlusions.
Results: A total of 661 EVAR procedures were carried out between 1996–2010. In 567 patients (56 female), both endograft limbs were deployed in the common iliac artery (CIA) leaving 94 patients (9 female) with at least one limb in the EIA. An adjunctive bare metal stent was used in 8 (9%) limbs deployed in the EIA. Seventeen (3%) limbs occluded in the CIA group compared with 14 (15%, $p < 0{\cdot}0001$) in the EIA group. The time to occlusion was 3 months (0–60) and 1 month (0–36) in the CIA and EIA groups, respectively. Limb occlusions were treated by femoro-femoral bypass (CIA group n = 16, EIA group n = 9), axillo-femoral bypass (CIA group n = 1, EIA group n = 2) and limb thrombectomy (EIA group only n = 3). No legs were amputated following occlusion of a limb placed in the CIA but there were three amputations in the EIA group ($p = 0{\cdot}045$). One patient died in each group.
Conclusion: Deployment of endograft limbs into the EIA led to a higher rate of occlusion and leg amputation. Increased tortuosity of the EIA, a smaller calibre vessel and the loss of internal iliac artery run-off are likely to account for the increased risk.

Endovascular repair of abdominal aortic aneurysms (AAA) with short and/or angulated necks: infra-renal sealing is not a safe option

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Objective: The options for endovascular repair of aortic aneurysms with a neck length of < 15 mm and angulation of > 60° (Cook Medical Inc. guidelines, 2003) are: 1) off-label use of an infra-renal device; and 2) use of a fenestrated endograft to extend the sealing zone proximal to the level of the renal arteries. In this paper we report the Results of treatment of aneurysms with adverse necks using infra-renal grafts.
Method: A large international EVAR registry database was interrogated to identify a population of patients that met the above definitions of 'adverse neck'. Outcomes were assessed specifically with respect to early Type 1 endoleak.
Results: Data from a total of 11,208 patients having endovascular repair of abdominal aortic aneurysms were reviewed. We identified 672 patients with a neck length of 14 mm or less and 2356 patients with angulation of > 60°. The total mean aneurysm diameter was 57·8 mm; mean diameter for short neck aneurysms was 59·9 mm and 62·6 mm for angulated necks. Overall, 2·8% of patients developed a proximal type 1 endoleak. The incidence of endoleak rate was 5·3% in angulated necks, 7·6% in short necks and 12·7% in aneurysms with both short and angulated necks.
Conclusion: Endovascular repair of abdominal aortic aneurysms with adverse necks using standard infra-renal endografts is associated with an unacceptable risk of proximal type 1 endoleak. The use of fenestrated endografts to extend the sealing zone proximal to the renal arteries is likely to be a better option for these patients.

Improving standards of care in AAA surgery: the patients' perspective

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Objective: The national QIP seeks to drive up the standard of care provided to patients with AAA. An important component of this work is a better understanding of patients' views.
Method: Patient groups were convened in five regions of the UK. A semi-structured focus group Methodology was used to define important areas for improvement.
Results: There were clear concerns across all patient groups about the lack of national assessment and treatment protocols (i.e. a national care pathway). Patient groups wish to see a consistent approach nationally to assessing the risks and benefits of surgery for individual patients. Communication from medical teams was felt to be inadequate particularly around postoperative care. There was perceived to be a lack of information, and that provided was over optimistic with regard to recovery from open surgery. Uncorrected unrealistic expectations led to anxiousness and discouragement in a slower recovery. There were conflicting views about centralization that mirror the current debate about configuration of vascular services. Patient groups were supportive of the development of networks as a means for managing complex cases by pooling expertise. There was interest in surgeons using simulators to practice difficult cases pre-operatively.
Conclusion: Vascular surgeons have much to gain from wider patient involvement in planning care. We believe that patient groups have a central role in defining national standards of care.

Use of baseline factors to predict serious complications and re-interventions after endovascular aneurysm repair (EVAR) in patients with a large abdominal aortic aneurysm: Results from the UK EVAR trials

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Objective: Data from the UK EndoVascular Aneurysm Repair (EVAR) trials were used to identify which factors are associated with the rate of graft-related complications and re-interventions after EVAR in patients with a large abdominal aortic aneurysm.
Method: Patients randomised to EVAR in either trial 1 or 2 were included providing they had undergone elective EVAR within 6 months of randomisation. Patients were followed by CT scans inspected by trial radiologists for graft-related complications and re-interventions. Analyses were timed from EVAR deployment and Cox regression (stratified by trial 1 or 2) was used to investigate whether any pre-specified anatomical or demographic factors were associated with time to first serious complication or re-intervention (type 2 endoleaks excluded).
Results: A total of 756 patients (588 EVAR trial 1) were followed for an average of 3·7 years, during which time there were 179 serious graft complications (rate 6·5 per 100 person years), and 114 re-interventions (rate 3·8 per 100 person years). The highest rate was during the first 6 months with an apparent increase again after 2 years. Multivariate analysis indicated that graft-related events increased significantly with larger aneurysm diameter ($p < 0{\cdot}001$) and older age ($p = 0{\cdot}04$). There was weaker evidence that patients with larger common iliac diameters experienced elevated complication rates.
Conclusion: Graft-related complication and re-intervention rates are high after EVAR in patients with a large aneurysm but younger patients and those with aneurysms closer to the 5·5 cm threshold for intervention experience lower rates. This bodes well for patients whose aneurysms are monitored in screening programmes until referral for repair at 5·5 cm.

Acute aortic syndrome (AAS) treated by thoracic endovascular aortic repair (TEVAR)

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Objective: Acute aortic syndrome (AAS) is a life-threatening condition and heralds imminent aortic rupture. Stent-graft repair offers a minimally invasive treatment solution and is becoming established as the treatment of choice for these patients. The Objective of this study was to evaluate the safety and mid- to long-term efficacy of thoracic endovascular repair for AAS.
Method: Consecutive patients presenting with AAS and treated with TEVAR were prospectively enrolled in a database and followed up at 3 months, then

annually thereafter. Death, stroke, paraplegia and secondary intervention were documented.

Results: 110 TEVAR were performed for AAS between 1997–2010. Seventy-five were men and 35 were women. The median age was 68 (18–90). Fourteen patients died (12·7%). The pathologies treated included acute complicated dissection (34 patients; 3 deaths); symptomatic aneurysm (29;5); infected aneurysm (16;3); transection (14;1); chronic dissection (8;1); others (9;1). The causes of death were aortic rupture (5), myocardial infarction (4), stroke (3) and sepsis (2). Seven (6·4%) patients became paraplegic with one death; 8 (7·3%) patients had a stroke with three deaths. The median follow-up was 44 months (1–153). Eleven patients (10%) had secondary procedures: 8 for Type I endoleak (3 conversion to open repair, 1 further stent-graft, 3 extension cuffs, 1 aortic banding), 2 for ongoing aortic infection (2 further stent-grafts) and 1 for aortic rupture (further stent-graft).

Conclusion: Acute aortic syndrome can be treated with thoracic endovascular repair with acceptable mid- to long-term Results. The secondary procedure rate demands vigilant postoperative clinical and imaging surveillance.

Use of CO_2 angiography for fenestrated endovascular aneurysm repair

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Objective: The development of fenestrated and branched EVAR is associated with increased usage of contrast and a significant incidence of postoperative renal dysfunction and renal failure has been reported. We describe the use of CO_2 as the primary contrast agent in patients undergoing complex EVAR.

Method: Two cohorts of patients undergoing fenestrated and branched EVAR were compared at a regional vascular unit. Sixty-one complex endografts were implanted between 2008 and 2010; 38 procedures were completed with only iodinated contrast media (group 1) and 23 utilised CO_2 as the primary contrast agent (group 2). The endpoint assessed was renal impairment, defined as an increase in creatinine of > 25%.

Results: Baseline creatinine was similar between group 1 (mean 109, range 44–282) and group 2 (mean 117, range 74–310). There was no significant difference in the incidence of postoperative renal dysfunction; however, 7 (18%) in group 1 required temporary dialysis, compared to just 2 (9%) in group 2 ($p = 0·056$). No patients required permanent dialysis. Further analysis between the groups demonstrated a reduction in mean volume of contrast used from 234 ml to 138 ml.

Conclusion: Renal impairment is a common postoperative complication amongst patients undergoing complex EVAR. The incidence of dialysis-dependent renal impairment is reduced by the use of CO_2 as a contrast medium.

Radiation exposure during endovascular treatment of the aorta: increased risk with complex repairs

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Objective: Exposure of the skin to radiation doses above 2 Gray (Gy) can cause burns. There is also an estimated excess lifetime cancer risk of 6% for every Sievert (Sv) of radiation absorbed. We measured patient radiation exposure during endovascular aortic procedures.

Method: Consecutive thoracic (TEVAR), infra-renal (IEVAR) and branched/fenestrated (BEVAR/FEVAR) aortic repairs carried out between 2003–2010 in a single centre were assessed. Indirect measurements of radiation dose (dose area product [DAP] and fluoroscopy time) were prospectively recorded with the C-arm dosimeter. Direct measurements of exposure at skin level (Gy) were obtained using Gafchromic dosimetry film. A whole-body effective dose (Sv) was calculated from DAP using PCXMC software.

Results: The TEVAR cohort (n = 232, age 71[15–89]), which included patients treated for aortic transection and dissections, were younger ($p < 0·0001$) than BEVAR/FEVAR (n = 53, age 76[58–85]) and IEVAR (n = 630, age 76[37–93]). Median DAP was higher ($p = 0·004$) in BEVAR/FEVAR compared with IEVAR and TEVAR: 32,060cGycm^2 [17,207–213,322] *versus* 17,300cGycm^2 [10,940–334,340] *versus* 19,440cGycm^2 [11,284–35,101], respectively. The equivalent skin doses were BEVAR/FEVAR: 1·3Gy (0·7–8·7); IEVAR: 0·7Gy (0·44–13·7); TEVAR: 0·8Gy (0·46–1·4). The effective whole-body doses were BEVAR/FEVAR: 0·096Sv (0·052–0·64); IEVAR: 0·053Sv (0·033–1·00); TEVAR: 0·058Sv (0·034–0·11). The skin dose exceeded 2Gy more often during BEVAR/FEVAR (31% of patients) compared with TEVAR (11%, $p = 0·005$) and IEVAR (11%, $p = 0·001$). The whole-body dose was > 1Sv in 4 patients (IEVAR = 3, TEVAR = 1).

Conclusion: Endovascular aortic procedures, in particular complex repairs, carry a substantial risk of skin damage. The excess malignancy risk is relatively small. Intra-operative image registration techniques should help to reduce the radiation dose.

Assessment of National Vascular Database (NVD) quality

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Objective: The NVD collects information on demographics and patient outcomes. Use for research is dependent on the ability to adjust for case-mix, which in turn depends on the completeness of data collected. We present data imputation techniques that allow missing data to be imputed (predicted) using the patient's known characteristics.

Method: AAA patients were selected from the NVD and were analysed for data completeness for the preferred and required fields. We have developed a model to predict the missing data by multivariate imputation by chained equations (MICE). The vascular biochemistry and haematology outcome model (VBHOM) was calculated on: (1) only patients with a complete data set; and (2) all patients using MICE imputation.

Results: 14,010 patients in the NVD-AAA data show that there is a range of missing data across variables (median 22%, interquartile range 10–64%). In particular, volume of cell salvage transfused, postoperative infections, and cardiovascular and renal events had missing data in excess of 50%. Geographical variation in missing data shows little variation amongst required fields (7%, 7–8%), but marked variation across fields not described as required or preferred (40%, 37–48%) and even greater variation amongst preferred fields (11%, 6–22%).

Conclusion: This analysis has identified hospitals with good data entry practices, and provides reassurance on the data quality in required fields; however, it also allows: (1) review of database design; and (2) the targeting of incomplete variables as a focus for the AAA QIP. Work is in progress to assess the effect of missing data on outcome models such as VBHOM.

Modifying the illness and treatment beliefs of patients with intermittent claudication increases daily walking and reduces demand for vascular intervention - Results from a randomised controlled trial

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Objective: Supervised exercise has been shown to increase pain-free walking distance and reduce symptoms of claudication. However, supervised exercise programmes are not widely available, require patient commitment to attend, and may not lead to lasting behaviour change beyond attendance at the programme. This trial (ISRCTN28051878) studied whether a brief psychological intervention to modify patients' beliefs about peripheral arterial disease and beliefs about walking would lead to increased walking and a reduction in the demand for vascular intervention.

Method: Sixty patients newly diagnosed with claudication were randomised into two conditions. The control condition received usual care, and the treatment condition received usual care and a brief psychological intervention to modify

illness and walking beliefs, and develop a walking action plan. Participants were followed up after 4 months. Daily steps were measured by pedometer.

Results: Participants in the intervention group had significantly increased ($p < 0{\cdot}01$) mean daily steps, while participants in the control group had decreased mean daily steps from baseline to follow-up. Participants in the control group were four times more likely ($p = 0{\cdot}009$) to opt for vascular intervention than participants in the psychological intervention group.

Conclusion: This trial demonstrates that a brief psychological intervention for patients with claudication can increase daily walking, and reduce the demand for surgery at this stage of the disease. This has implications for the design of services to treat patients with intermittent claudication.

Modelling the effect of venous disease upon quality of life

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Objective: A clear understanding of the relationship of venous reflux, clinical venous disease and the effects upon quality of life (QoL) has eluded researchers. This study aims to illustrate the impact of venous disease and observe the incremental direct effect upon QoL. Commissioning bodies are progressively withdrawing funding for interventions; evidence of the impact of venous disease must be sought.

Method: Consecutive patients were assessed and those with isolated, unilateral, single superficial axial incompetence were included. Clinical grading was performed with the CEAP and Venous Clinical Severity scores (VCSS). Patients completed generic (SF36 and EQ5D) and disease-specific (Aberdeen Varicose Vein Questionnaire - AVVQ) QoL instruments. Multivariate regression modelling was performed, controlling for demographic and anatomical factors, to elucidate the association of clinical severity upon QoL impairment.

Results: 456 patients with C2-6 disease were included along with control data for 105 people with C0-1 disease. Increasing clinical grading corresponds strongly with deterioration in disease-specific QoL ($p < 0{\cdot}001$). This is stratified into C0-1, C2-4 and C5-6 disease ($p < 0{\cdot}001–0{\cdot}006$). Increasing clinical grading also corresponds with deterioration in the physical domains of SF36 ($p < 0{\cdot}001–0{\cdot}002$), along with index utility scores (SF6D and EQ5D $p < 0{\cdot}001$). This was apparent from C2 disease, where the reported impact of pain was comparable with reference cases suffering with angina, whereas the physical impairment seen with ulceration was comparable with that seen in congestive cardiac failure and COPD.

Conclusion: Significant demonstrable morbidity is seen even with uncomplicated venous disease. This provides strong support for the continued funding of interventions to address this QoL impairment.

A prospective double-blind randomised controlled trial of radiofrequency *versus* laser treatment of great saphenous varicose veins

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Objective: Endovenous ablation of varicose veins using radiofrequency (RFA) and laser fibres (EVLT) has reported advantages over traditional open surgical treatment. There is little evidence comparing the efficacy and patient-reported outcomes between the two endovenous solutions. This study compares the RFA and EVLT strategies in a prospective double-blind clinical trial.

Method: Consecutive patients with primary unilateral great saphenous vein (GSV) reflux undergoing endovenous treatment were randomised to RFA or EVLT. The primary outcome measure was GSV occlusion at 3 months following treatment. Secondary outcome measures were occlusion at 7 days, postoperative pain, analgesic requirement and bruising, assessed at day 7 following surgery. Quality of life (QoL) was assessed pre-operatively and 3 months following surgery using the Aberdeen Varicose Vein Questionnaire (AVVQ) and EQ-5D.

Results: 159 patients were randomised to RFA (79 patients) or EVLT (80 patients). Groups were well matched for demographics, disease extent, severity and pre-operative QoL. Duplex scanning confirmed 100% vein occlusion at 1 week in both groups. At 3 months, occlusion was 97% for RFA and 96% for EVLT; $p = 0{\cdot}67$. Median (IQR) percentage above-knee bruise area was greater following EVLT 3·85% (6·1) compared to RFA 0·6% (2); $p = 0{\cdot}0001$. Postoperative pain assessed at each of the first 7 postoperative days was less after RFA ($p = 0{\cdot}001$). Changes in the AVVQ ($p = 0{\cdot}12$) and EQ-5D ($p = 0{\cdot}66$) at 3 months were similar in both groups.

Conclusion: RFA and EVLT offer equivalent venous occlusion rates at 3 months following treatment of primary GSV varices. RFA is associated with less peri-procedural pain, analgesic requirement and bruising.

Combined medical therapy and carotid endarterectomy for asymptomatic stenosis: 10-year stroke prevention in ACST-1

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Objective: In a randomised trial (ACST-1) of 3120 asymptomatic patients with severe carotid narrowing comparing early with deferred carotid endarterectomy (CEA), CEA significantly reduced 10-year stroke risk. All other aspects of patient treatment were left to the discretion of the clinician. Throughout the trial antithrombotic and antihypertensive drugs were widely used but use of lipid-lowering therapy increased substantially. We examined the influence of different medical treatments on the overall stroke prevention effect of the trial.

Method: Use of lipid-lowering, antithrombotic and blood-pressure-lowering medical therapies was recorded at randomisation, 4 months and at yearly intervals for 10 years. Time-dependent analysis of event rates was compared between trial groups.

Results: From 1993 to 2003, antiplatelet drugs were taken by around 90% patients (with another 8–9% taking anticoagulant treatment instead), and most (~90%) patients were taking blood-pressure-lowering agents by the end of follow-up. Lipid-lowering therapy usage increased rapidly (to > 80%). Stroke rate ratio (immediate CEA vs deferred) appeared similar for those on all three therapies and those not, but because absolute stroke rates were lower among those on lipid-lowering therapy, absolute difference in annual stroke rate for those allocated immediate CEA was not as great. Overall, stroke risk was reduced by about a third and, as with other analyses, there was additional (~6% ARR) stroke prevention benefit in those who had early CEA.

Conclusion: Event rates among those currently on lipid-lowering therapy suggest somewhat lower peri-operative risks and lower absolute benefits, but still with a significant reduction in net risk at year 10 (9·6% vs 14·5%, absolute difference 5·0%).

Clinical assessment pre-CABG identifies patients at risk for postoperative stroke

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Objective: The management of incidental carotid stenosis in patients undergoing coronary artery bypass grafting (CABG) remains controversial. Our cardiac unit refers patients for carotid duplex if they have one or more of: bruit, known cerebrovascular disease, known stenosis or amaurosis fugax. The aim of this study was to investigate the benefit of such a policy.

Method: Patients undergoing CABG without valve surgery over a 3-year period (2007–9) were identified. Patients undergoing carotid duplex scanning, carotid interventions, and patients who suffered a peri-operative stroke (not TIA) were identified from vascular and stroke databases.

Results: 3076 patients (2368 male; median 68 years; range 35–88) underwent CABG. 105 patients (3·4%) were referred for carotid duplex (89 male; median 70 years; range 49–85); of these, 8% were normal carotid arteries, 70% had < 75% carotid stenosis, 17% had > 75% carotid stenosis and 6% had carotid occlusion. Seven patients with > 75% carotid stenosis (7/18 identified) underwent endarterectomy, one pre-CABG and six combined procedures. Thirty-nine patients (1·27%) suffered a stroke within 30 days of surgery. The stroke rate was 8/105 (7·6%) in scanned *versus* 31/2971 (1·04%) unscanned

patients (Chi-squared $p < 0{\cdot}0001$). There were no strokes in CEA patients. Nor did any patient with non-operated > 75% stenosis suffer a stroke.

Conclusion: Simple clinical assessment identified a patient group at increased risk of CABG-related stroke. As no stroke patient in this group had a > 75% carotid stenosis, strategies other than CEA are required to reduce this stroke rate.

The burden of carotid endarterectomy (CE) complications - underneath stroke and death

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Objective: CE is increasingly undertaken urgently and has potential significant complications. Our aim was to analyse the complication profile of CE especially in relation to undertaking the procedure urgently - rapid access carotid endarterectomy (RACE).

Method: Data were collected prospectively on consecutive CEs recording age, sex, presentation, anaesthetic, operation, surgeon, and outcome. Patients were evaluated by stroke physicians routinely pre and post-op at 30 days, 6 months and 1 year. All complications were meticulously recorded and classified.

Results: There were 255 CEs (166 elective; 89 RACE) from August 2007 to August 2010 and 84% were uncomplicated. Complications included death 3 (1·2%; 1 within 30 days from a bleeding DU [RACE], 2 after 30 days from an MI [RACE] and chest infection after fits from hyperperfusion syndrome-elective), peri-op stroke 3 (1·2%) and TIA 2 (0·8%), hyperperfusion syndrome 3 (1·2%), haematoma 9 (3·6%; 5 drained, 4 managed conservatively), nerve injury to the hypoglossal nerve 6 (2·3%) and recurrent laryngeal nerve 5 (1·9%), intra-operative complications 4 (1·6% which were prolonged bleeding, fits and conversion to GA) and other 6 (2·4% such as hyper/hypotension, arrhythmia, urinary retention, etc). There was no significant difference between elective CE and RACE for death or individual complications but there was significant difference ($p = 0{\cdot}04$; Fisher's Exact Test) with relatively more minor local/general complications in elective 21 (Vs RACE 9) and more significant complications/death in RACE 8 (Vs Elective 2).

Conclusion: These findings have important implications for consent, considering that even with a 30-day death rate of 0·4% and stroke rate of 1·2%, still 16% of patients experienced some complication. Not unexpectedly, RACE had more significant complications but rates were low making it still worth undertaking.

Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: data from the EVAR trials

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Objective: Graft rupture after EVAR has been reported, often preceded by graft-related complications. Graft rupture also has been reported after open repair. The aim was to assess rate and factors associated with rupture after endovascular (EVAR) or open repair (OR) of abdominal aortic aneurysm.

Method: By July 2009, a total of 848 elective EVARs and 594 elective ORs had been performed in the United Kingdom EVAR trials 1 and 2. Patients have been followed for complications, re-interventions and rupture. The incidence of rupture was explored in relation to baseline anatomy and subsequent complications in a Cox regression analysis.

Results: There were no ruptures in the OR patients. A total of 27 ruptures occurred after EVAR during a mean follow-up of 4·8 years: crude rate = 0·7 [95% CI 0·5–1·0] ruptures per 100 person-years. Eighteen patients (67%) died within 30 days of rupture. Five ruptures occurred in the first 30 postoperative days and 22 after that: crude rates of 7·2 [95% CI 3·0–17·4] and 0·6 [95% CI 0·4–0·9] per 100 person-years, respectively. Previous complications (endoleak types 1, 2 with sac expansion, 3, migration or kinking) increased the risk of rupture, adjusted hazard ratio 8·83 [95% CI 3·76–20·76], $p < 0{\cdot}0001$.

Conclusion: There were no ruptures after OR and a low rate after EVAR. Mortality after graft rupture is high and previous serious complications are significantly associated with the risk of rupture. Few ruptures after EVAR appear to be spontaneous without complications identified during optimal surveillance.

A prospective study of the natural history of deep vein thrombosis: early predictors of poor late outcomes

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Objective: A proportion of patients with deep vein thrombosis (DVT) will develop post-thrombotic syndrome (PTS). Currently, the only clearly identified risk factors for developing PTS are recurrent ipsilateral DVT and extensive proximal disease. It is difficult to predict early on which patients will run into trouble. The aim of the study was to find better predictors of poor clinical outcome following a DVT.

Method: Patients with suspected acute DVT in the lower limb were assessed prospectively. All patients with a confirmed DVT were asked to participate in this study. Within 7–10 days following diagnosis of DVT, patients underwent a further review, involving clinical, ultrasound and air plethysmography assessment of both lower limbs. Patients were re-assessed at regular intervals for 5 years.

Results: 122 limbs in 114 patients were enrolled. Thrombus regression occurred in two phases, with a rapid regression between 10 days and 3 months, and a more gradual regression thereafter. Four risk factors for PTS were identified as best predictors: clot load on presentation (> 10), at 6 months < 50% lysis, venous filling index > 2·5 mL/sec and abnormal outflow rate (< 0·6). Patients with 3 or more of these risk factors had a significant risk of developing PTS with sensitivity 100%, specificity 80% and positive predictive value 55%. Patients scoring 2 or less were normal.

Conclusion: This is the first study which has shown that venous assessment at 6 months post-DVT can predict PTS at 5 years. Those who will not develop PTS can be reassured of this at 6 months.

Flow-sensitised dynamic magnetic resonance imaging (MRI) can identify dominant false lumen flow and secondary entry tears in type B aortic dissection: implications for endovascular treatment

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Objective: Endovascular repair is established as the treatment of choice for complicated type B dissection. Current imaging can identify primary but not secondary entry tears making device length and accurate placement difficult. This may result in continued false lumen perfusion requiring multiple re-interventions to prevent aortic dilation and rupture. The Objective was to visualise and quantify blood flow in the true and false lumens to determine the location and contribution of entry tears in type B aortic dissection.

Method: Twenty patients with type B aortic dissection underwent magnetic resonance imaging at 3T. High resolution 3D anatomy images (inversion-recovery-3D-SSFP [resolution = 1·0 mm^3, FA = 20°, TI = 350 ms, TR/TE = 4·0/1·3 ms, TFE-factor = 22]) were obtained using gadofosveset trisodium. Multi-directional blood flow information was acquired using time-resolved 3-directional phase contrast MRI (FA = 10°, TR/TE = 5·0/2·7 ms, 25 cardiac-phases, VENC[FH/RL/AP] = 150 cm/s). Flow-velocity time curves were derived using semi-automatic segmentation algorithms.

Results: The primary entry tear was identified in all patients. The velocity of blood flow was greater in the true lumen compared to the false lumen (mean difference 16·58 cm/s, $p < 0{\cdot}0001$ [95% CI 13·58–19·57]). In six patients (30%) the false lumen was the dominant flow system. In all patients false lumen flow was complex with high levels of backward and regurgitant flow (mean regurgitant fraction (%)[SD] = 29·42[27·13]). Changes in false lumen blood volume and regurgitant fraction indicated the position and contribution of secondary entry tears.

Conclusion: Flow-sensitised dynamic MRI is able to identify dominant false lumen flow and the location and contribution of entry tears in type B aortic dissection. This information will improve endovascular device sizing and placement, and result in improved clinical outcome.

Further evidence for the role of patch angioplasty (PA) over primary closure (PC) during carotid endarterectomy (CEA)

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Objective: Despite concerns about data quality/poor trial design the 2009 Cochrane review concluded that PA (n = 1076) compared to PC (n = 932) reduces ipsilateral peri-operative stroke (IS) risk with trends towards lower 'any stroke' (AS) and all-cause mortality (ACM) during CEA. This has been investigated further in an unrelated RCT of 3438 CEA patients with symptomatic or asymptomatic carotid stenosis.
Method: A 30-day independent neurological review assessed primary outcome events. Risk ratios were calculated comparing PA (n = 1588) with PC (n = 1850: 985 conventional [PCC], 712 eversion [PCE], 153 unspecified [excluded]). PA and PC data were then combined with Cochrane data.
Results: There were no differences in demographic data, ASA status, carotid stenosis, comorbidities, and anti-thrombotic use between the groups. Operative time was less for PC (81 v 107 min, p = 0·001). Odds ratios (± 95% confidence intervals) for PA *versus* all PC suggested no benefit for PA (IS: 0·98, 0·66–1·45; AS: 0·94, 0·66–1·33; ACM: 1·76, 0·97–3·17 [trend favouring PC]). However, when PCC (IS: 0·82, 0·52–1·28; AS: 0·82, 0·52–1·23) and PCE (IS: 1·19, 0·70–2·03; AS: 1·26, 0·78–2·03) are considered separately, trends favour PA over PCC and PCE over PA. Combining PA and PCC with Cochrane data strengthens the role for PA (IS: 0·62, 0·42–0·90, p = 0·016; AS: 0·73, 0·52–1·02) in stroke reduction although the trend for PCC reducing ACM (1·09, 0·6–1·95) persists.
Conclusion: When data from a much larger study (with independent neurological review) is combined with the Cochrane data, the role for PA over PCC is stronger. However, PCE may offer similar benefits to PA with shorter operating times.

Distal bypass grafts in patients with critical leg ischaemia with poor pedal arch

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Objective: To evaluate the amputation-free survival and patency rates of distal bypass grafts in critical leg ischaemia (CLI) in the presence of a complete or incomplete pedal arch.
Method: A retrospective analysis of all patients with CLI undergoing distal bypass between January 2004 and April 2010 was conducted. Kaplan-Meier analysis was used to assess and compare amputation-free survival and patency rates at 12 months.
Results: 129 consecutive patients (98 men, median age 76, range 19–96) underwent 144 distal bypasses. The incidence of diabetes mellitus and renal failure was 69% and 29%, respectively. 92% had a vein conduit and 8% a PTFE + Miller cuff. Out of 144 bypasses, 24 (17%) had a complete pedal arch (CPA), 40 (28%) had a dorsal pedal arch (DPA) only, 39 (27%) had a plantar pedal arch (PPA) only, 27 (19%) had no pedal arch (NPA), and 14 (10%) of cases could not be assessed due to inadequate images. In-hospital mortality was 2·1%. The amputation-free survival (AFS), primary, assisted primary and secondary patency rates for all four pedal arch groups at 1 year were: CPA: 84%, 63%, 95% and 95%; DPA: 73%, 61%, 88% and 88%; PPA: 84%, 52%, 84% and 90%; NPA: 78%, 52%, 87% and 87%.
Conclusion: Amputation-free survival and patency rates are comparable in all groups. The authors would therefore advocate distal bypass grafts in patients with CLI in the presence of a complete or incomplete pedal arch.

The risk of occlusion and associated events in the Asymptomatic Carotid Surgery Trial: a 10-year prospective study

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Objective: This study analyzes the risk of occlusion and associated neurological events in patients with severe asymptomatic carotid artery stenosis included in the ACST-1 trial.
Method: In ACST-1, 3120 patients were randomised between immediate surgery or deferral of CEA. During the study 198 patients developed occlusion of the internal carotid artery and we evaluated the associated neurological events. Patients with contralateral occlusion at baseline were excluded from analysis. Kaplan-Meier analysis was performed to estimate freedom from occlusion and occlusion-related stroke-free survival.
Results: Mean follow-up was 80·8 months (range 0–165 months); 144 ipsilateral and 54 contralateral occlusions (immediate: 38 vs. 33, p < 0·01) occurred in 198 patients. Occlusion-free survival rates at 1, 5 and 10 years were 98%, 95% and 94% in the immediate CEA group, and 97%, 91% and 88% in the deferred CEA patients. The likelihood of occlusion was significantly greater (p < 0·01) in the deferred group. Risk of symptomatic occlusion after 5 and 10 years was lower (0·5% and 0·7% *versus* 1·7% and 2·5%, respectively) in the immediate *versus* deferred groups. Nineteen patients developed an occlusion-related stroke. The overall stroke-free survival rate in patients with occlusion at 1, 5 and 10 years was 99·5%, 96·7% and 86%, respectively.
Conclusion: This long-term follow-up analysis shows that occlusion occurred more often in patients in whom CEA was deferred. Overall stroke-free survival did not differ between patients with or without occlusion.

Laparoscopic aortic aneurysm surgery: early experience from three UK vascular centres

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Objective: Laparoscopic aortic aneurysm surgery is an alternative or adjunct to open or endovascular repair and may confer certain advantages. We report our early experience of laparoscopic aortic aneurysm surgery.
Method: Peri-operative and postoperative data and outcomes were recorded prospectively on consecutive patients undergoing elective laparoscopic-assisted or total laparoscopic aortic surgery at three vascular centres.
Results: Following a period of formal mentorship, 64 patients with infra-renal aneurysmal disease including 43 aortic and 21 aortoiliac (6 juxtarenal) aneurysms, underwent surgery. Sixty were male with a median age of 72 years (range 58–88). Median aortic diameter was 6·0 cm (IQR 5·7–6·5). Thirty-eight patients had laparoscopic-assisted surgery (2 required conversion to an open procedure) and 26 had total laparoscopic surgery. Median aortic clamp time was 95 minutes (IQR 75–126) with a median operative time of 355 minutes (IQR 315–395). Median postoperative epidural requirement was 1 day (range 0–3); median time to return to solid diet was 1 day (range 1–6) and median time to mobilisation was 1 day (range 1–4). Median postoperative hospital stay was 6 days (range 2–98). One patient died within 30 days (1·6%) and 13 (20%) developed early complications. Following a median follow-up of 24 months, 4 developed late complications (4 incisional herniae) with no late graft-related complications seen.
Conclusion: Laparoscopic aortic aneurysm surgery may be performed with a low peri-operative mortality and good early durability. By comparison with open surgery early operative times were long, epidural usage was limited, recovery of gut function and mobility was early and length of stay was short.

Renal function in patients following open repair of Type IV thoracoabdominal aneurysms: long-term Results

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Objective: Limited longitudinal data exist on the effect of open repair of suprarenal aortic aneurysms on renal function.
Method: Consecutive patients undergoing repair of Crawford Type IV thoracoabdominal aneurysms over a 10-year period were included in a retrospective cohort study. Pre-operative, discharge and most recent estimated glomerular filtration rate (eGFR) were examined alongside survival.
Results: Eighty-two patients of median (range) age 69 (21–77) years underwent aneurysm repair. Five (6%) patients died in hospital and a further 19 (23%) died over a median (range) follow-up of 25 (1–125) months. Pre-operatively, 45 (56%) patients had an eGFR > 60 ml/min, 36 (43%) patients had an eGFR 15–60 ml/min and one (1%) patient an eGFR of < 15 ml/min. On discharge, 42 (54%) patients had an eGFR > 60 ml/min, 33 (42%) had an eGFR 15–60 ml/min and three (4%) had an eGFR < 15 ml/min. During follow-up, 11 (26%) of the 42 patients with an eGFR > 60 ml/min on discharge died, 24 (57%) were still alive with no change in renal function, 6 (15%) had deteriorated to an eGFR 15–60 ml/min, and 1 (2%) had an eGFR < 15 ml/min. Of 32 patients with an eGFR 15–60 ml/min on discharge, 6 (19%) died, 7 (22%) returned to an eGFR > 60 ml/min, and the remaining 19 (59%) patients had an eGFR 15–60 ml/min. Two (67%) of the three patients discharged with an eGFR < 15 ml/min died, and the other recovered to an eGFR 15–60 ml/min.
Conclusion: Open suprarenal aneurysm repair can be performed safely with minimal adverse effect on long-term renal outcome.

Assessment of scoring for high-risk patients undergoing endovascular aneurysm repair

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Objective: The 10-year follow-up Results of the EVAR 1 and EVAR 2 trials have shown no difference in all-cause mortality when the patients are followed up over a longer period. Similar Results were seen in the DREAM trial. These Results highlight that there are some high-risk patients who may not be benefiting from endovascular intervention. A group from New York has suggested scoring to define this high-risk group based on comorbidities (age, sex, renal failure, peripheral vascular disease, pulmonary, cardiac and neurological problems) and experience. We have applied this scoring to our patients who underwent EVAR to assess the validity of this scoring system.
Method: We retrospectively analysed all the patients who had an EVAR for an infra-renal aneurysm and scored them on the proposed scoring.
Results: 202 patients had EVAR between December 1997 and March 2010. Overall 30-day mortality was 3·96%. 96% of the patients had a score of 9 or less. 30-day mortality for patients with scores of 0–4 was 1·4%, for a score of 5–8 was 7·7%, for a score of 9–10 was 11·1% and for a score of 11 or more was 33·3%.
Conclusion: Although our numbers are small the Results are very similar to the Results from the Medicare data on which this scoring has been proposed. We therefore propose that this is a valid scoring system and should be considered to define high-risk patients undergoing EVAR.

A pre-operative model for predicting mortality risk in elective AAA surgery

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Objective: A reliable pre-operative prediction of risk for elective AAA repair would be valuable to surgeons and patients. A multivariate risk prediction model for 30-day mortality following elective open and endovascular abdominal aortic aneurysm (AAA) repair has been developed using the Vascular Governance North West (VGNW) database.
Method: Prospective data on 2765 consecutive patients undergoing elective open or endovascular AAA repair from Sept 1999–Oct 2009 was randomly split into development (n = 1936) and validation datasets (n = 829). Logistic regression analysis was undertaken using a forward-stepwise technique to identify risk factors for 30-day mortality.
Results: Variables associated with 30-day mortality (n = 98, 5·1%) in the development dataset included: anti-platelet medication ($p < 0.001$), female gender ($p = 0.002$), open surgery ($p = 0.002$), age ($p = 0.005$), creatinine ($p = 0.006$), diabetes ($p = 0.029$) and respiratory disease ($p = 0.031$). The receiver operating characteristic (ROC) curves for predicted probability of 30-day mortality in the development and validation datasets were 0·73 and 0·70, respectively. The model showed good calibration in both datasets. Observed *versus* expected 30-day mortality in the validation dataset (50 [6%] deaths) for low, medium and high-risk groups was 3·2% v 2·0%, ($p = 0.27$), 6·1% v 5·1%, ($p = 0.67$) and 11·1% v 10·7%, ($p = 0.88$), respectively, with no significant difference between observed and expected mortalities.
Conclusion: This multivariate model predicted 30-day mortality following elective AAA repair across all risk groups particularly when mortality risk is high. Surgeons may find it useful to calculate patient-specific risk for case mix adjustment of their Results and in the consent process. Validation against the National Vascular Database is now necessary.

Aortic aneurysm repair in octogenarians

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Objective: We report the Results of abdominal aortic aneurysm (AAA) repair, postoperative complications and 30-day mortality, in octogenarians in the North West of England.
Method: Data were collected prospectively on all patients undergoing AAA repair at 22 hospitals between September 1999 and May 2010.
Results: AAA repair was perfomed in 575 patients aged > 80 and 3314 patients aged < 80. The mean AAA diameter was 7·0 cm in octogenarians and 6·7 cm in patients aged < 80 ($p < 0.001$). Elective repair was performed in 390 (68%) octogenarians, urgent repair in 51 (9%) and emergency repair in 134 (23%); mortality rates were 11·3%, 17·6% and 53·0%, respectively. These were significantly higher than the equivalent rates in patients aged < 80 of 4·7%, 8·7% and 28·9% ($p < 0.001$). Octogenarians were more likely to be female (25% v 16%) or have emergency surgery (23% v 18%), dyspnoea (35% v 28%), an abnormal ECG (39% v 29%), haemoglobin < 13g/dL (42% v 29%), or creatinine levels > 120 µmol/L (31% v 19%) ($p < 0.05$). They were less likely to have a history of ischaemic heart disease (34% v 38%) or to be taking a statin (30·8% v 41·4%) ($p < 0.05$). Risk factors associated with increased 30-day mortality in octogenarians by multivariate analysis were: non-elective repair, supra-renal AAA and creatinine levels ≥ 150 µmol/L. Compared to patients aged < 80, octogenarians were more likely to suffer postoperative myocardial infarction (8·0%), respiratory failure (16·9%) and renal failure (13·9%) ($p < 0.05$).
Conclusion: The risk of mortality and morbidity following AAA repair is higher in octogenarians. Careful patient selection is essential. The standard threshold of 5·5 cm for elective AAA repair is inappropriate at this age.

Growth rate of very small aneurysms

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Objective: The UK national screening programme for aortic aneurysms has recommended no follow-up for aneurysms less than 30 mm in AP diameter. The aim of this study was to examine the growth rate of aortic aneurysms up to 30 mm diameter.
Method: A personal database, collected over 16 years, of 693 patients with a small aortic aneurysm < 55 mm was searched for those presenting with an aneurysm < 31 mm. The growth rate of this group was examined.

Results: Sixty-six patients had an AAA < 31 mm in AP diameter at first scan. All patients had at least two further measurements. Twelve aneurysms were < 25 mm, 35 were 25–27 mm and 19 were 28–30 mm at first scan. The growth rate for the whole group was 1·65 mm/y (0–6·5 mm) and for the three groups 1·42 (0–3·3), 1·85 (0·3–5·0) and 1·44 mm/y (0–6·5), respectively. In only 2 patients did the aorta not grow at all. The rate of growth was not related to the diameter at first measurement being on average 6·32%, 7·08%, and 5·04%, respectively, for the three groups.
Conclusion: Small aortic aneurysms less than 31 mm grow at much the same rate as those between 30–55 mm. The UK aneurysm screening programme should reconsider its decision not to follow up this group of patients.

Early experience of the UK aneurysm screening programme

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Objective: The UK Multicentre Aneurysm Screening Study (MASS) provided evidence of the benefit from screening for abdominal aortic aneurysms (AAA). In view of these findings, the national AAA screening programme was recently introduced. We report our findings from the initial screening period in Southwest London, an early implementation screening site.
Method: A retrospective analysis was performed on data collected from all patients since the onset of the screening programme. Men aged 65 were invited to attend an ultrasound assessment as per the national protocol. Self-referrals (men aged > 65) were also scanned.
Results: The total target population was 10,593. 6,091 males were invited between April 2009 and June 2010. 4,216 were screened including 162 self-referrals (mean age 72·5 yrs). 2,037 (33·4%) failed to attend. Of those scanned, 4,136 (98·1%) had aortic diameters less than 3·0 cm, including 24 (0·6%) with diameters 2·6–2·9 cm. Seventy-five (1·8%) had aneurysms 3·0–5·4 cm, and 5 (0·1%) had aneurysms 5·5 cm and above. Aneurysms were identified in 1·7% of those invited, and 6·2% of the self-referral group. Of all 80 aneurysms, 79 were found in white males, while 1 (3·0 cm) was found in a black male of Caribbean origin.
Conclusion: The prevalence of AAA is lower in this cohort than expected. Limiting invitations to 65-year-olds, a diverse patient population and the high rate of non-attendance are likely causative factors. Current aneurysm identification rates may have an impact on the cost-effectiveness of the screening programme, and further research may be justified to identify those 65-year-olds most likely to have an AAA.

Aneurysm screening Results in North London - a world away from the MASS trial

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Objective: In January 2009, the Royal Free Hospital began screening for AAA in advance of the national programme. The case for national screening was based, in large part, on the Results of the 2002 MASS trial. Here we compare our data with that reported in the MASS trial.
Method: Men aged 65 in North London were identified by their GP practice and invited for an abdominal aortic ultrasound. In addition, men or women who fell outside the criteria or catchment area were allowed to self-refer for a scan.
Results: 2346 patients were invited for scanning (1/5 self-referred). The mean age was 66·5 vs 69·2 in MASS. 93% were men over 65, 6% were men 60–64 (with a large skew to age 64), and < 0·2% were women or men under 60. Ethnicity (where given) was 1337 white, 328 non-white (not given in MASS). The social deprivation categories included the more deprived than average vs the less deprived than average in MASS. A total of 1665 of 2346 were scanned (71%) vs 27,147 of 33,839 (80%) in MASS. Total aneurysms detected were 13 vs 1333 in MASS. The prevalence of AAA was 0·78% of scans vs 4·9% of scans in MASS ($p \ll 0.01$). The 99% CI of AAA prevalence was 0·13–1·43% vs 4·5–5·3% in MASS. The breakdown of positive scans by aneurysm size was: 3 cm to 4·4 cm: 7; 4·5 cm to 5·4 cm: 2; > 5·5 cm: 4 (prevalence 0·25%).
Conclusion: The prevalence of AAA is six-fold lower in North London than in the MASS trial population. Excluding men under 65 and women makes no meaningful difference to the analysis. The reasons for this are unclear. However, the difference certainly impacts on the cost-effectiveness of screening, and deserves further study.

Prevalence of screen-detected AAAs in men aged 65 is decreasing; however, the prevalence of cardiac and respiratory diseases remains significantly higher in this group

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Objective: To study the prevalence of AAAs and major cardiac and respiratory diseases in men aged 65 attending a local AAA screening programme.
Method: Between 2001 and 2008, all 65-year-old men attending a local screening programme covering a population of 450,000 were given a questionnaire to complete prior to their aortic scan. Information regarding history of ischaemic heart disease, cardiac failure, hypertension, stroke, diabetes and chronic respiratory disease were collected. Data were analysed using cumulative moving averages analysis and Pearson's x2 test where appropriate.
Results: Over the study period, 17,362 men were invited. Of these, 13,982 (80·5%) attended for a scan and completed their questionnaires. 389 men were found to have an AAA. A gradual decline in AAA average prevalence from 3·2% to 2·65% (17% reduction) was observed. This was associated with a decline in the prevalence of each of cardiac disease (6%), stroke (21%) and chronic respiratory disease (28%). The prevalence of pre-diagnosed hypertension increased by 16% and that for diabetes by 21%. When compared to men with normal aortic diameter, men with AAAs had a higher prevalence of each of cardiac disease (31·99% vs 16·80%, p0·000), chronic respiratory disease (16·71% vs. 11·22%, p0·022), hypertension (52·35% vs 38·06%, p0·000) and stroke (7·89% vs. 3·55%, p0·067).
Conclusion: In the population studied, a noticeable decline in AAA screening yield was observed. Whilst a reduction in the prevalence of major cardiovascular and respiratory diseases was also observed, the prevalence of these diseases remains significantly higher in AAA patients. These findings suggest that a combined strategy of earlier risk factor modification and later invitation for AAA screening may improve overall AAA disease management.

Establishing a volume-outcome relationship in lower limb bypass surgery using multi-level logistic regression modelling

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Objective: A volume-outcome relationship is known to exist for abdominal aortic aneurysm and carotid endarterectomy surgery. We sought to investigate if such a relationship exists for lower limb arterial bypass surgery in the UK.
Method: All femoro-popliteal bypass operations performed in England between 2002–2006 were identified from Hospital Episode Statistics data. A Charlson type risk profile, including operating hospital annual case volume, was identified for each patient. Outcome measures of revision bypass, amputation, death and a composite measure were established during the index admission and at 1 year. Multivariate modelling allows adjustment of results for significant determinants of outcome. Multi-level modelling adjusts for hospital trust level variations, including hospital volume, and therefore highlights significant variations in outcome between Trusts.
Results: 25,133 popliteal bypass operations were identified. There were significant differences in outcome between NHS Hospital Trusts for repeat bypass ($p = 0.005$), major amputation ($p < 0.001$), in-hospital mortality ($p = 0.001$) and the composite measure ($p < 0.001$) with multi-level modelling. An increase in hospital volume by 50 bypass procedures per year reduced the odds of major amputation (OR 0·969, 95% CI 0·939–0·999, $p = 0.043$), death (OR 0·972, 95% CI 0·949–0·996, $p = 0.024$) and the composite outcome (OR 0·978, 95% CI 0·956–0·999, $p = 0.042$) during the index admission. At 1 year, an increase in volume decreased the chances of death or amputation (OR 0·980, 95% CI 0·965–0·995, $p = 0.0110$).

Conclusion: Variation in outcomes after lower limb bypass surgery exist between hospital Trusts. Hospital annual case volume is a significant factor in this variation, although the benefits are modest.

Outcome in the management of acute diabetic limb emergencies - a revolving door?

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Objective: An 'ideal' outcome in acute diabetic limb salvage may be defined as a patient who is discharged without a major amputation and has complete wound healing within a year without any unplanned readmissions. We examined the effect of a multidisciplinary approach in the pursuit of this composite outcome.
Method: A retrospective study of consecutive emergency admissions for acute diabetic foot complications was performed for the period between 1st Aug 2007 to 1st Aug 2009. Outcomes analysed included in-hospital mortality, limb salvage, wound healing and re-admission rates at 12 months.
Results: Ninety-four patients (male 66% with 95% Type 2 diabetes) were identified with a median age of 75 years (46–96). Median LOS was 24 days (1–233). Risk factors were smoking (54%), hypertension (62%), peripheral arterial disease (70%), ischaemic heart disease (30%) and chronic kidney disease (30%). Baseline median HbA1c levels were 7·7% (5·4–15·5). 98% presented with tissue loss (55% Wagner classification between 2 to 5). Medical therapy on admission included statins (86%), antiplatelets (77%), ACE inhibitors (53%), beta-bockers (20%) and antibiotics (94%). Thirty-seven limbs were revascularised - endoluminal (57%) and bypass surgery (43%). Initial amputation rates were minor amputations (30%) and major amputations (8·5%). In-hospital mortality was 8·5%. At 12 months, amputation-free survival was 70%. Only 49% of patients were alive without amputation and ulcer free at 12 months. When re-admissions were included the composite 'ideal' outcome was achieved in only 22% of all patients.
Conclusion: Although acceptable limb salvage rates are achievable, a significant proportion of patients presenting with acute diabetic limb emergencies suffer the 'revolving door' experience of incomplete wound healing and high re-admission rates despite a multidisciplinary team approach.

Training of future vascular surgeons in the UK in endovascular techniques is inadequate to train vascular specialists of the future. Results of a survey of UK vascular trainees

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Objective: Vascular surgery training for the future will require acquisition of skills in endovascular techniques and vascular ultrasound. This study aims to determine the current exposure of vascular trainees in the UK to this training.
Method: An email survey of 169 trainees, identified from the Association of Surgeons in Training database, with a declared vascular surgery interest was performed. Data were collected on experience in EVAR, peripheral endovascular interventions (PE) and vascular ultrasound (US).
Results: The response rate was 49% (83/169) from 89% of training regions in the UK. Trainees performed EVAR top-graft deployment (41·5%), contralateral limb cannulation (44·6%), and limb deployment (63·1%) in their current unit. 30·8%, 32·3% and 20%, respectively, had never performed these procedures. Vascular trainees gained experience of PE for iliac (25·8%), SFA (22·7%), and infrapopliteal (13·6%) intervention. 63·6%, 71·2%, and 86·2% have never performed PE. Trainees performed some arterial duplex in 29% of units, of which 70·8% are unvalidated. Venous duplex at outpatient clinics is performed by surgical consultants or trainees scan in 42% of units. Trainees feel they are not being trained in EVAR planning (30·1%), EVAR techniques (24·7%), PE (58·9%), and US (69·9%). Endovascular simulator training is available to 6·8%. 83·6% feel vascular surgery is unable to meet training expectations. The largest obstacle was felt to be lack of engagement of radiologists (60·6%).
Conclusion: Current training of vascular surgeons in the UK in endovascular techniques is insufficient to provide skills required to deliver specialist care, and to allow training of vascular specialists of the future.

Secondary medical prevention among Danish patients hospitalized to primary vascular surgery

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Objective: To analyse the use of secondary medical prevention among Danish patients hospitalized for primary vascular reconstruction between 1996 to 2006, with special attention to age differences.
Method: The nationwide Danish Vascular Registry was the main source of data, facilitated by other nationwide databases via the unique civil registration number. We assessed the proportion of prescriptions for secondary medical prevention in pre-defined time periods after surgery. To describe age differences we used logistic regression analysis, (age sub-groups 40–59, 60–79, and > 80), adjusted for gender, socioeconomic variables, marital status and comorbidity.
Results: 17,943 were included; 54·5% were males with a mean age of 68·8 years (range 40–99). Drugs prescribed during the entire period were as follows: lipid-lowering drugs 59·7%, anti-thrombotic drugs 84·3%, ACE/ATII antagonists 55·8%, and beta-blockers 45%. The proportion declined for all examined drugs throughout all pre-defined time periods; the exceptions were lipid-lowering drugs and anti-thrombotic therapy. This tendency was clearest in patients > 80 years. Patients > 80 years had an increased chance of receiving a prescription for beta-blockers (OR 1·31 [1·14;1·51]), anti-thrombotic therapy (OR 1·19 [0·99;1·44]), ACE/ATII (OR 1·48 [1·29;170]) and a decreased chance for lipid-lowering drugs (OR 0·62 [0·54;0·72]) compared to the age group of 40–59 years.
Conclusion: Prescription rates of examined secondary medical prevention were low in our study compared to national and international guidelines. A general decline of repeat prescriptions was observed over time, largest in the oldest part of the population, who must be expected to have the biggest comorbidity. Ongoing efforts to implement cardiovascular prophylactics are crucial, especially in elderly patients with symptomatic peripheral arterial disease.

The impact of standard treatment on balance and physical function among claudicants

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Objective: Intermittent claudication is associated with deficiencies in physical function that may contribute to impaired balance and a higher risk of falls. Hence the aim of this study was to assess balance in claudicants undergoing treatment with exercise or angioplasty.
Method: A concurrent prospective case series study was carried out with two treatment arms of angioplasty (PTA) or a 12-week supervised exercise programme (SEP). Ninety-eight patients were recruited, 51 underwent SEP and 47 underwent PTA. All were assessed for severity of ischaemia and balance using the Sensory Organisation Test (SOT, NeuroCom).
Results: Both groups were comparable in terms of age, gender and comorbidities. The severity of ischaemia was significantly worse in the SEP group with lower ABPI and shorter initial treadmill walking distances ($p < 0·05$, Mann Whitney U). At baseline, abnormal balance was seen in 46 patients (47%), comprising 28/51 SEP and 18/47 PTA (55% and 38%, respectively). At 3 months there was a significant improvement in the number of patients with normal balance in the SEP group (23/51 improved to 34/51; $p < 0·05$, Chi squared); however, the PTA group showed no such improvement (29/47 at baseline *versus* 30/47 at 3 months; $p > 0·05$).
Conclusion: Balance impairment is prevalent among older claudicants. Treatment of claudication with angioplasty makes no impact on this impairment, but supervised exercise leads to significant gains in balance despite their increased

severity of ischaemic disease. Greater consideration to exercise programmes for claudicants should be addressed particularly in view of the potential to improve possible fall risk.

Incidence and survival outcome following femoral artery reconstruction during endovascular abdominal aortic aneurysm repair

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Objective: Planned or unplanned reconstruction of the common femoral artery (femoro-femoral crossover and/or patch closure) may be required following endovascular abdominal aortic aneurysm (EVAR) stent-graft deployment for arterial closure or maintenance of lower limb perfusion. However, the incidence and impact on postoperative survival of such procedures is unknown. The aim of this study was therefore to determine the incidence of common femoral artery reconstruction (FAR) following EVAR and examine the effect of such procedures on patient outcome.

Method: 178 patients undergoing EVAR were studied retrospectively.
Results: Thirty-one patients (17·4%) underwent FAR; 16 (51·6%) femoro-femoral crossover and 15 (48·4%) endarterectomy and patch closure. There was no significant difference in postoperative complications ($p = 0·057$) or 30-day survival ($p = 0·454$) between patients undergoing FAR and direct closure of the femoral arteries. However, long-term all-cause survival in patients undergoing femoral artery reconstruction was significantly poorer than those undergoing direct closure (Log rank $Chi^2 = 6·588$, DF = 1, $p = 0·010$). On forward conditional regression analysis three factors - the need for FAR (HR = 0·435, $p = 0·006$), COPD (HR = 0·424, $p = 0·002$) and AAA size (HR = 1·414, $p = 0·005$) - were significantly and independently associated with survival.
Conclusion: FAR was performed in almost one in five patients undergoing EVAR and was significantly and independently associated with decreased survival. This effect did not seem related to the procedure itself, and may be a reflection of increased atherosclerotic disease in this group of patients. Multidisciplinary teams should be aware of these findings when planning EVAR, especially in borderline candidates.