Letters to the editor

Radial artery spasm during cardiac angiography: the impact of endothelial dysfunction and anxiety

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The radial artery is a common access site for coronary catheterisation owing to reduced risk of bleeding complications.[1] However, the procedure is often complicated by the occurrence of radial artery vasospasm, which necessitates patients to be exposed to the alternative, less preferential femoral route catheterisation. This increases the duration of the procedure, and may increase vascular complications.[2] In a study of 379 patients undergoing radial artery catheterisation, the outer sheath diameter of the catheter along with radial artery diameter were among the independent predictors of vasospasm.[3] Furthermore, administration of vasodilator agents glyceryl trinitrate and sodium nitroprusside did not reduce the risk of vasospasm. Indeed, there is a possibility that the catheter may cause disruption of the endothelial cell lining resulting in endothelial dysfunction – an inflammatory response characterised by the loss of the vasodilator, nitric oxide, along with concomitant increase in vasoconstrictive factors, such as endothelin-1 or thromboxane.[4] However, despite administering potent vasodilators, vasospasm still occurred, suggesting that factors other than loss of vasodilatation could contribute to the vasoconstrictive effect.

A recent line of enquiry has concerned the impact of patient anxiety on the clinical severity of spasm. In their study of 81 patients indicated for coronary angiography, Ercan et al.[5] reported that higher anxiety (using Hamilton Anxiety Scale) was associated with radial artery vasospasm, particularly in females. Other studies report that anxiety is common before, during and after coronary angiography procedures.[6–8] Moreover, showing informative videos before coronary angiography reduces anxiety levels,[9] and guided imagery before surgery can reduce mean anxiety levels.[10] Indeed, there has been much research since the 1980s evidencing the anxiety-ameliorating potential of psychological intervention both in pre- and post-operative environments.[11–13] Collectively, these findings suggest that alternative mechanisms might impact on the vasculature, and it seems plausible that anxiety (or any form of stress) will increase sympathetic innervation to the vessel via activation of α-adrenoreceptors located in the vessel.[14] It is our view that further prospective studies are required to elucidate the mechanisms responsible for vasospasm in patients undergoing coronary angiography. Such studies need to incorporate robust methodology, including assessments of endothelial function in the microvasculature and large vessels, examination of anxiety and inclusion of large sample size. Furthermore, appropriately powered randomised control trials could examine the long-term impact of techniques used to reduce anxiety on the vasculature.

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Behçet's disease and bipolar disorder

Hibberd et al. emphasise bipolar disorder as an associated feature of Behçet's disease (BD).[1] Talarico et al. recently reported on psychiatric involvement in 116 patients with BD and compared them to a control group of patients with systemic lupus erythematosus (SLE) and chronic hypertension.[2] The BD cohort was divided in two groups depending on the presence or otherwise of neurological features. The frequency of bipolar disorder was significantly higher in the BD cohort than in disease controls ($p < 0.001$). However, there was no significant difference in unipolar depression and insomnia in the BD, SLE and chronic arterial hypertension groups. In addition, the presence of bipolar disorder in BD patients (mainly hypomanic episodes) was not related to the presence of neurological involvement; however, the presence of manic bipolar disorder was associated with active disease.

The higher frequency of psychiatric manifestations in BD adds to the importance of a multidisciplinary approach to patients. A clinical psychologic or psychiatric input is important. The recently published EULAR recommendations for the management of BD need to be updated to include management of psychological aspects of the disease.[3]

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Liquorice (*Glycyrrhiza glabra*): the journey of the sweet root from Mesopotamia to England

The beguiling story of liquorice in its many aspects as told by Lee[1] struck several chords with this correspondent, partly because of a boyhood fondness for Liquorice Allsorts, partly because of the previous use of liquorice in asthma treatment, but principally because of recently visiting the old ducal town of Uzes in the Gard department of south western France. Uzes is the source of the Roman aqueduct whose UNESCO World Heritage stretch is the Pont du Gard. Uzes may have had knowledge of liquorice since the Arab–Islamic extension from Spain into France in the eight century.[2] The town has a liquorice factory, set up by Henry Lafont in 1862. It has been owned by the German company Haribo since 1985 and now also boasts the Haribo liquorice museum. Among the artists who created posters to advertise the liquorice products in the 1880–1910 period were Henri Toulouse-Lautrec and poster designer and painter Leonetto Capiello, reputedly the father of the modern advertising poster. Nowadays, however, Capiello, unlike Toulouse-Lautrec, appears to have almost disappeared into the ether of art history. It is noted also that Haribo now owns a liquorice factory in Pontefract, an ironic twist of history considering the destructive impact of the Luftwaffe on the Ewbank's factory. As Lee shows the sweet root (and the industry of which it is the raison d'etre) is indeed well travelled. It had the capacity to survive, as it endured the long hazardous return from Mesopotamia to medieval France and England. The outward leg of this journey was well documented by the explorer and historian Tim Severin,[3] who followed on horseback the route of the great crusader Godfrey de Bouillon, first ruler of the Kingdom of Jerusalem. Liquorice also survived the dissolution of the monasteries, as well as assault from the air in the Second World War, and assault on the ground by government regulation as happened in Britain in 1939. The liquorice industry also survived allegations in 2017 of exploitation of carnuaba wax workers in Brazil. Carnauba wax is a resin derived from the leaves of the palm tree *Copernicia prunifera* and is sometimes used as a surface smoothing and antisticking agent in liquorice and other gums. Accordingly, the task of trekking with the sweet root from Mesopotamia, and its preservation from the eleventh into the twenty-first century, appears to have been a sometimes not very sweet experience. Nevertheless the images evoked by this historic story, such as horseback Crusaders and siege towers at the gates of Jerusalem,[3] as well as that of the intrepid monks of Cluny carting (and sailing) their precious booty all the way from the banks of the Euphrates to Pontefract, are well worth savouring.

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'Working diagnosis' as a means to reduce cognitive bias

O'Sullivan and Schofield gave an excellent summary of the problem of cognitive bias in the diagnostic process.[1] Metacognition and use of Bayesian theory were highlighted as means to mitigate the effect of bias. We suggest that the routine use of the term 'working diagnosis' would draw attention to these strategies by emphasising the uncertainty that prevails. Even when all relevant tests have been made, some uncertainty may remain. The task of the clinician is, therefore, not necessarily to attain certainty, but rather to *reduce the level of diagnostic uncertainty enough to make optimal therapeutic decisions*.[2] It is accepted clinical practice to compile a list of differential diagnoses – these each have

varying degrees of plausibility. The 'working diagnosis' is simply the differential with the greater probability. By using the term 'working diagnosis', the clinician is challenged to re-evaluate the diagnosis in light of new evidence. In this way, anchoring bias, confirmation bias and premature closure bias may be avoided. Clinicians should embrace uncertainty whilst avoiding decision paralysis in the face of uncertainty.

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Positive facets of simulation-based learning: patient safety, risk management, synergy with e-learning and its use in life support courses

I read with interest, Simulation in Medical Education by So et al.[1] in which the authors have advocated in favour of using simulation-based learning (SBL) as a delivery method in medical education. I would like to bring certain interesting points regarding SBL to the reader's attention. SBL has been used as a risk management strategy in different healthcare systems around the globe and evaluations have indicated favourable outcomes to support its use in this regard.[2] SBL can be applied as learning modality to improve patient safety in healthcare settings and has a benefit of being able to be tailored to the needs of learners, whilst allowing for deliverable positive outcomes and cost effectiveness.[3] SBL is being used around the world but there has been a special emphasis on its use in the NHS in the UK, as it has been seen as a way of delivering patient-centred high-quality education to NHS staff to improve patient safety and risk manage serious incidents.[4,5] Certain education centres in the UK have even won international awards in recognition of their success in delivering world-class simulation training in healthcare.[5] Simulation has been widely used in the delivery of life support courses, such as basic life support, advanced life support, advanced cardiac life support, advanced trauma life support and paediatrics advanced life support by Resuscitation Council UK [RC (UK)], European Resuscitation Council (ERC) and American Heart Association (AHA), as simulation improves learner confidence, performance and communication.[6] It will be very interesting to note if RC (UK), ERC and AHA could come forward with some results from the wealth of data available to them to further confirm the findings available in the literature regarding SBL. Another interesting facet of SBL is its association with e-learning that has shown to improve the utilisation and outcomes of SBL when used jointly with e-learning modules.[7] This approach of using e-learning in conjunction with simulation training has been used by many mainstream organisations utilising SBL during their standardised courses, for example during life support courses organised by RC (UK), ERC and AHA.[8–10]

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Authors' reply

We are happy to see the letter from Malik with supplementary information of how simulation can lead to effective medical education. We agree that there are many ways in which simulation can be applied to improve the quality and safety of healthcare. Although our paper[1] focused on education and training, simulation is a very effective form of assessment as demonstrated by the popularity of objective structured clinical examinations in both postgraduate and undergraduate education.[2] Simulation can be used for research into topics that are difficult to study in an authentic clinical environment. One good example is the demonstration of the effectiveness of using surgical-crisis checklists.[3] Finally, simulation can be used for evaluating how different elements of a system interact with each other, such as whether facilities or equipment are well designed for human use.[4,5] We agree that simulation should be used more frequently to enhance quality and safety in healthcare.

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Relationship between acute asthma, pneumomediastinum and pulmonary embolism

When acute asthma is complicated by pneumomediastinum, as in the recently reported case[1] and in one other report,[2] symptoms such as retrosternal chest tightness[1] and pleuritic chest pain[2] may simulate those documented in pulmonary embolism (PE). Furthermore, PE can present with severe wheezing simulating acute severe asthma,[3] and asthma appears to increase the risk of pulmonary thromboembolism.[4] The latter observation was made in a nationwide case–control study that included 114,366 Swedish-born patients with a first hospital admission of PE, 76,494 with deep vein thrombosis (DVT) and 6,854 with combined DVT and PE, between 1981 and 2010. In each group asthma was included as a comorbidity. Each case was matched with five controls for age, sex and educational level. Asthma was found to be associated with an adjusted odds ratio for PE amounting to 1.43 [95% confidence interval (CI), 1.37–1.50), for DVT amounting to 1.56 (95% CI, 1.47–1.65) and for combined DVT and PE 1.60 (95% CI, 1.32–1.93).[4] PE may, itself, be complicated by pneumomediastinum, due to septic cavitation of a pulmonary infarct situated adjacent to the mediastinal pleura.[5] In the latter context the management of pneumomediastinum includes antibiotics to mitigate the risk of mediastinitis.[5] Accordingly, in the event of the occurrence of PE-related pneumomediastinum in a patient with asthma the strategy of watchful expectancy employed in some cases of pneumomediastinum[1,2] needs to be complemented by prophylactic antibiotics to mitigate risk of mediastinitis.

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Authors' reply

We thank Dr Jolobe for his interest in our recent paper[1] and highlighting the link between airways disease and thrombosis. It is true that recent studies have shown that asthma is a risk factor for pulmonary embolism[2–4] and can pose a diagnostic challenge in clinical practice, especially when patients present with acute asthma symptoms. It is not entirely clear about the mechanism of the association, but both local and systemic inflammation inducing prothrombotic effects[5–8] and the use of steroids that leads to endothelial dysfunction are hypothesised.[9,10] Further studies are needed to evaluate the various mechanisms in hypercoagulability in asthma patients.

Pneumomediastinum secondary to a pulmonary embolism and subsequent acute mediastinitis is extremely rare and usually is a sequelae of septic cavitation complicated by pulmonary infarction. However, this seldom leads to chronic or fibrosing mediastinitis.

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