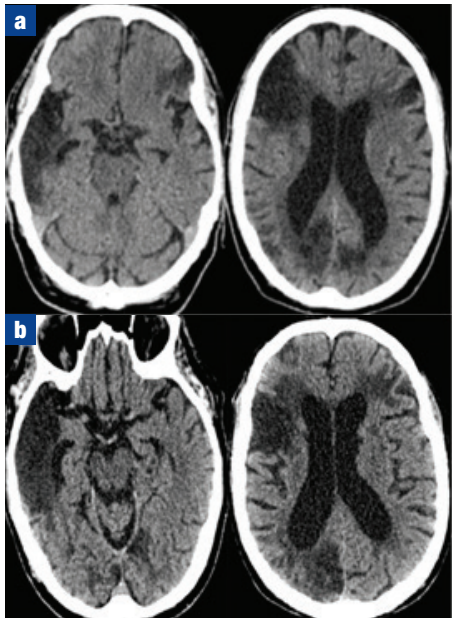
Apixaban for stroke prevention in a patient with a mechanical heart valve

Introduction

Patients with mechanical heart valves require lifelong anticoagulation to prevent valve thrombosis and thromboembolic complications without increasing the risk of bleeding. Currently, only vitamin K antagonists are licensed for thromboprophylaxis in patients with a mechanical heart valve. The substitution of vitamin K antagonists by direct oral anticoagulants is not recommended.

Figure 1. Comparative axial view of computed tomography scan of the head from **(a)** 2015 and **(b)** 2017 showing multiple bilateral cortical and subcortical infarcts in both anterior and posterior circulations. There were no new infarcts on the most recent scan.



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This article describes a 75-year-old man with a mitral mechanical heart valve who presented with a fall, left hemiparesis and dysphasia. He had stopped taking warfarin over a year earlier and had had multiple cerebral ischaemic strokes. After exploring options, the patient elected to take apixaban for anticoagulation. Over 2.5 years later he has not had any further ischaemic strokes.

Discussion

Patients with mechanical heart valves require lifelong thromboembolic prophylaxis with a vitamin K antagonist (Baumgartner et al, 2017). Mechanical mitral valves carry twice the risk of thromboembolism than aortic valves. In the absence of anticoagulation, the risk of thromboembolism is about 4% per year, and vitamin K antagonists reduce this to 1% (Cannegieter et al, 1994). There have been three cases of patients with long-term non-anticoagulated mitral mechanical heart valves and these were considered to be the result of good luck or genetic variations (Salmane et al, 2016) (factors which did not apply in the current patient).

CASE REPORT

A 75-year-old man presented with a fall, left hemiparesis and dysphasia of indeterminate onset time.

His medical history included implantation of a mitral mechanical heart valve along with coronary artery bypass graft in 2010 while living in Australia and he was anticoagulated with warfarin. However, in 2014, following an internet search and concluding that warfarin was a rat poison he ceased taking it but continued taking aspirin.

A detailed neurological examination elicited left upper and lower limb weakness, left facial weakness, left hemianopia and dysphasia. The cardiovascular examination revealed the closing click of the mitral mechanical heart valve.

An urgent computed tomography scan of the brain demonstrated an acute left pons ischaemic stroke along with bilateral multiple chronic anterior and posterior circulation ischaemic strokes (*Figure 1a*). He was assessed swiftly but because of the indeterminate time of onset, he was not considered for thrombolytic treatment. His aspirin dose was increased to 300 mg.

Transthoracic echocardiography showed a normal functioning metallic mitral valve without thrombosis. Magnetic resonance imaging of the brain was not performed because of the presence of the metallic heart valve.

He steadfastly refused to take warfarin despite attempts to educate him that this was the only licensed thromboprophylaxis available for patients with a mechanical heart valve. He was deemed to have capacity according to the Mental Capacity Act 2005. Although there have been no previous reports of this, the authors explored the hypothetical idea of cardiothoracic intervention to replace the metallic valve with tissue, but he was against this.

He was not averse to taking other anticoagulants such as direct oral anticoagulants. At that time, the authors had just heard about the premature termination of the RE-ALIGN trial as a result of excessive thromboembolic and haemorrhagic concerns.

Two cardiologists and the trust's legal advisor were consulted about the use of direct oral anticoagulants. Understanding the scenario they agreed that, if the patient agreed, apixaban might be the best available option. The authors discussed the option of apixaban with him and his son, and explained that it had never been used in a patient with a mechanical heart valve before, as well as informing them about the premature withdrawal of the RE-ALIGN trial. After due consideration, the patient opted to go ahead with the proposal. Approval was obtained from the local formulary committee for the use of apixaban. As this was an individual case ethics approval was not obtained. Written consent was also obtained from the patient, and he was commenced on apixaban 5 mg twice daily.

He was discharged home with the early supported discharge team. He has been reviewed for over 2.5 years, and has not had any thromboembolic or haemorrhagic complications. His most recent computed tomography brain scan did not show any new ischaemic lesions (*Figure 1b*), although he has become cognitively impaired because of the significant ischaemic burden.

The RE-ALIGN trial compared dabigatran with warfarin in patients with mechanical heart valves but was terminated prematurely because of excess thromboembolic and haemorrhagic events in the dabigatran arm (Eikelboom et al, 2013). Other direct oral anticoagulants may be effective, but there will be no substitute for vitamin K antagonists in patients with mechanical heart valves for the foreseeable future.

A meta-analysis comparing trial and real-world data on haemorrhagic complications of direct oral anticoagulants and vitamin K antagonists in patients with non-mechanical heart valves found fewer haemorrhagic complications with direct oral anticoagulants (Chai-Adisaksopha et al, 2014). At the time the current patient was being treated, based on consensus and the experience of the treating clinicians, apixaban was commenced. Real-world data suggest that, of the direct oral anticoagulants, apixaban has a better bleeding profile (Lip et al, 2016).

It is hoped that this article may pave the way for future trials on factor Xa inhibitors as this patient remained free from thromboembolic events close to 2.5 years after initiation of apixaban. **BJHM**

Baumgartner H, Falk V, Bax JJ et al; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017 Sep 21;38(36):2739–2791. https://doi.org/10.1093/eurheartj/ehx391

Cannegieter SC, Rosendaal FR, Briët E. Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. Circulation. 1994 Feb 01;89(2):635–641. https://doi.org/10.1161/01.CIR.89.2.635

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Lip GYH, Keshishian A, Kamble S, Pan X, Mardekian J, Horblyuk R, Hamilton M. Real-world comparison of major bleeding risk among non-valvular atrial fibrillation patients initiated on apixaban, dabigatran, rivaroxaban, or warfarin. Thromb Haemost. 2016 Aug 19;116(5):975–986. https://doi.org/10.1160/TH16-05-0403

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LEARNING POINTS

- Patients with a mechanical heart valve require lifelong thromboprophylaxis using a vitamin K antagonist.
- Direct oral anticoagulants are not licensed for use in patients with mechanical heart valves, but this case may encourage trials of factor Xa inhibitors in these patients.
- Internet medicine is informative but can lead patients to making unwise decisions.
- Imparting effective medical information to patients may avoid unnecessary internet consultation.

Giant hydronephrosis presenting as acute pyelonephritis

A usually fit and well 49-year-old man presented to hospital with a 5-day history of malaise and suprapubic pain. Clinical examination revealed tenderness and fullness of the right flank. Urine dipstick was positive for nitrites and leukocytes. Blood tests revealed raised C-reactive protein (294 mg/litre), creatinine (136 µmol/litre) and urea (10.2 mmol/litre) levels. The patient was treated with intravenous piperacillin-tazobactam.

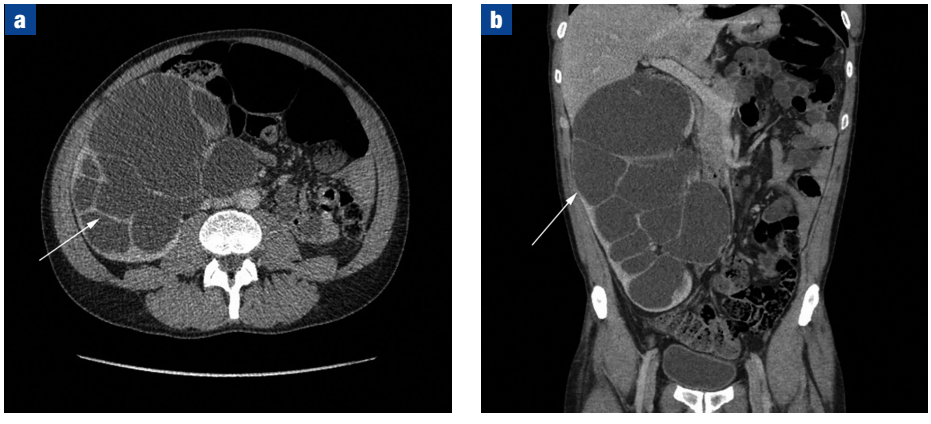
Ultrasound of the renal system revealed a large fluid-filled mass confirmed on computed tomography as a giant hydronephrotic right kidney (*Figure 1*). Radionuclide scan of the right kidney revealed poor function. Laparoscopic nephrectomy was performed 3 months later with an uneventful recovery. The patient has now returned to work.

Giant hydronephrosis is defined as a kidney with more than 1 litre of fluid accumulated in the renal collecting duct (Stirling, 1939) and in the majority of adult cases arises as a result of chronic obstruction at the pelviureteric junction (Sataa et al, 2011). **BJHM**

Sataa S, Kerim S, Ben Rhouma S et al. Giant hydronephrosis in adults: what is the best approach? Retrospective analysis of 24 cases. Nephrourol Mon. 2011;3(3):177–181.

Stirling WC. Massive hydronephrosis complicated by hydroureter: report of 3 cases. J Urol. 1939;42:520–533. https://doi.org/10.1016/S0022-5347(17)71549-2

Figure 1. a. Axial and **(b)** coronal image from computed tomography of the abdomen showing giant septated right kidney with marked cortical thinning (arrows), measuring 13x19x25 cm.



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