# Letters to the editor

OVERVIEW

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## Beware of thromboembolic risk in obese patients on direct oral anticoagulants (DOACs)

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Editor – We read with interest the article by Burden *et al* on pulmonary embolism in a patient on rivaroxaban and concurrent carbamazepine.[1] While the authors highlight the interaction between rivaroxaban and carbamazepine, one should be mindful of other risk factors that might reduce the therapeutic efficacy of a direct oral anticoagulant (DOAC), namely severe obesity, possibly due to suboptimal dosing regime in such patients.

We encountered an elderly woman with severe obesity (body weight: 120.95 kg, body mass index [BMI] 44 kg/m$^2$] who presented with pleuritic chest pain. She was taking apixaban 5 mg twice daily for atrial fibrillation. CT pulmonary angiogram confirmed an acute pulmonary embolus. There were no other risk factors and we felt that the reason for her suboptimal anticoagulation was severe obesity as this could have led to higher volume of distribution and lower mean peak concentration of apixaban.[2] We stopped the apixaban and treated her with warfarin.

Studies using DOACs have had fewer obese or morbidly obese patients and only a few had analysed the effect of weight on the pharmacokinetic and pharmacodynamic properties of DOACs. Results indicated that patients with higher body weights had lower peak concentrations, increased volume of distribution and shorter half-lives of DOACs.[3,4]

Although dose adjustment of DOACs in severely obese patients are still not recommended on the product literature, expert guidance suggests avoiding DOACs in patients with a BMI of >40 kg/m$^2$, or a weight of >120 kg.[4] If DOACs are used in such patients, they recommend checking drug-specific peak and trough levels and substituting it with a vitamin K antagonist if the levels are below the expected range, rather than adjusting the DOAC dose.[4]

It is important to raise awareness of clinicians on this matter as venous and arterial thromboembolic events while taking DOACs account for 3–5% of adverse events that are reported to the Medicines and Healthcare products Regulatory Agency (MHRA).[5] While there is a need for more data on the efficacy of DOACs on obese patients, we also need guidance on the most appropriate anticoagulation regime for patients who suffer a thromboembolic episode despite being on a DOAC. ■

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### References

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2 Upreti VV, Wang J, Barrett YC *et al*. Effect of extremes of body weight on the pharmacokinetics, pharmacodynamics, safety and tolerability of apixaban in healthy subjects. *Br J Clin Pharmacol* 2013;76:908–16.
3 Güler E, Güler GB, Demir GG, Halipoğlu S. A review of the fixed dose use of new oral anticoagulants in obese patients: Is it really enough? *Anatol J Cardiol* 2015;15:1020–9.
4 Martin K, Beyer-Westendorf J, Davidson BL *et al*. Use of direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. *J Thromb Haemost* 2016;14:1308–13.
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## Which crystalloid? Does fluid choice influence patient outcomes in sepsis?

Editor – I read with interest the informative review by Tidswell and Singer regarding the definition, pathophysiology, diagnosis and management of sepsis.[1]

The article correctly highlights that the issue of fluid choice for patients with sepsis is a key dilemma for both researchers and clinicians. The authors suggest that there is little to recommend one crystalloid over another as first-line resuscitation fluid.

Two recent studies have added to the increasing body of evidence that balanced crystalloid solutions are associated with improved outcomes compared to 0.9% saline for all patients.[2,3] These support existing evidence focusing exclusively on patients with sepsis, indicating better outcomes in patients managed with balanced crystalloids.[4]

There are clear limitations to the available evidence and studies vary according to inclusion criteria, design and outcome measurement. Any treatment choice must take into account patient-specific factors such as serum potassium levels and further research is needed to facilitate informed clinical decision making. However, it would appear that currently the balance of evidence is tipping in favour of balanced crystalloids and against 0.9% saline as the optimal resuscitation fluid for most patients. ■