Regardless of the designation employed for this neoplasm, we believe reporting this case can be helpful in calling this issue to the attention of others, with the hope that additional cases will be reported and perhaps lead to a consensus for the optimal terminology for cases such as that described in this report.

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Anti-Xa levels with low molecular weight heparin calibrator can be used to exclude significant apixaban effect

Sir,

Apixaban levels can be measured using an anti-Xa assay with apixaban-specific calibrator. However, as apixaban levels are infrequently required and the specific calibration and control material has limited stability at room temperature, the commitment of resources to perform an apixaban level may not be deemed justifiable at some laboratories. Therefore, they may not offer the assay, or limit availability to restricted hours of operation. In contrast anti-Xa levels for low molecular weight heparin (LMWH) are more commonly requested, and easier to perform after hours. We sought to correlate apixaban levels with anti-Xa-LMWH, with the aim of identifying a threshold anti-Xa-LMWH level that would allow exclusion of therapeutic apixaban levels in emergency situations.

We collected blood from 28 patients who had been taking apixaban for at least 3 days, and performed anti-Xa using STA-Liquid Anti-Xa kit with STA-Multihep calibrator and STA-apixaban calibrator (Stago, France). The demographic data are shown in Table 1, and the correlation curve is shown in Fig. 1.

At lower levels of apixaban, there is a near-linear relationship between apixaban level and anti-Xa-LMWH. These findings are consistent with previous studies demonstrating a linear relationship between anti-Xa-LMWH activity and apixaban levels in this range measured using either liquid chromatography tandem mass spectrometry (LC-MS/MS) or an apixaban-calibrated anti-Xa assay.[1–3] The 'on target' range for apixaban is quoted as being 20–100 ng/mL for 2.5 mg twice daily dosing and 30–412 ng/mL for 5 mg dosing twice daily.[4–6] According to our results, 20 ng/mL correlates with an anti-Xa-LMWH of 0.40 IU/mL. Hence, an anti-Xa-

Table 1 Demographics

Apixaban dose	2.5 mg BD	5 mg BD	All samples
n	17 (61%)	11 (39%)	28 (100%)
Gender, *n*			
Male	11 (65%)	5 (45%)	16 (57%)
Female	6 (35%)	6 (55%)	12 (43%)
Age, years			
Median	66	59	65
Range	47–83	18–87	18–87
Weight, kg			
Median	88	76	81
Range	55–128	50–130	50–130
Creatinine clearance, mL/min			
Median	84.1	100.4	93.2
Range	39.8–115.5	50–136.1	39.8–136.1
Time since ingestion, hours			
Median	7.25	7.42	7.25
Range	4.4–8.75	5–10.17	4.4–10.17
Apixaban level, ng/mL			
Median	48.5	100.9	70.3
Range	21–143.3	30.8–202.5	21–202.5

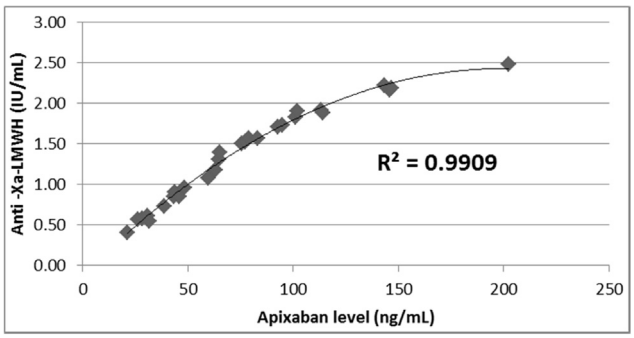

Fig. 1 Anti-Xa-LMWH versus apixaban level.

LMWH result of less than 0.40 IU/mL, for example in a patient going for emergency surgery, can be reassuring that the apixaban level is very low. Our findings are consistent with those of a recently published study.[7] Therefore, when no apixaban level is available it would be reasonable to use an anti-Xa-LMWH assay to exclude significant apixaban effect in emergency situations.

A similar approach has also been proposed for rivaroxaban.[8] As illustrated in the correlation curve, the relationship between anti-Xa-LMWH and apixaban levels becomes non-linear as apixaban concentration increases, and therefore anti-Xa-LMWH activity is not a suitable alternative for reliably quantitating apixaban. Furthermore, there is variability between absolute anti-Xa-LMWH activity reported with different commercial reagents and studies.[8,9] Ideally laboratories should develop their own cut-offs with their own reagents if using anti-Xa-LMWH to exclude apixaban. Importantly, it should also be confirmed that the patient has been receiving apixaban rather than rivaroxaban, as rivaroxaban will also be detected but may have a different cut-off point for exclusion using anti-Xa-LMWH. Conversely, both apixaban (Fig. 1) and rivaroxaban have greater anti-Xa activity than that seen with a similar therapeutic dose of LMWH,[1–3] so even a small amount of apixaban or rivaroxaban significantly interferes with attempts to measure enoxaparin activity by anti-Xa assay.

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ACTH measurements in Cushing's syndrome: the need for caution and communication

Sir,

Adrenocorticotropic hormone (ACTH) concentration levels are key in determining the cause of Cushing's syndrome. However, the assay may be vulnerable to interference. This report discusses the case of a 40-year-old woman with cortisol excess and unilateral adrenal lesion but elevated ACTH concentration suggestive of ACTH-dependent Cushing's syndrome. Through close collaboration with the chemical pathology team, it was determined that assay interference was likely leading to a falsely elevated ACTH concentration. The patient underwent a successful unilateral adrenalectomy and avoided further unnecessary testing.

A 40-year-old Chinese woman was referred to the endocrinology outpatient clinic for investigation of an incidentally discovered left adrenal mass and elevated random serum cortisol. On questioning, she reported 2 years of lethargy, central adiposity, and easy bruising as well as amenorrhoea for the previous 3 months. She had no headaches or visual changes. She had suffered from low back pain. She had no relevant family history and took no prescribed or alternative medications. She was a life-long non-smoker and worked in an administrative role.

On clinical examination, her weight was 67 kg and she was normotensive (BP 120/80 mmHg). She had the classical Cushingoid appearance of moon facies, buffalo hump and central adiposity and when compared to photos from 5 years prior, the physical changes were marked. There was no significant abdominal striae or thin skin.

Repeat computed tomography (CT) of her adrenal glands demonstrated a stable left 31 × 24 mm adrenal adenoma with heterogeneous contrast enhancement (non-contrast 22 and post-contrast 126 Hounsfield units) unchanged compared to imaging 18 months ago. Functional testing for primary hyperaldosteronism and phaeochromocytoma was negative.