How often do routine ICU coagulation tests become abnormal?

Forbes McGain, Madeline Corke, Fabien Dade, Riley Hazard, Dominique Grant and Craig French

Limited evidence exists of patient benefit consequent to ordering routine daily intensive care unit (ICU) blood tests.[1-3] Their conduct may potentially have negative impacts, including anaemia, discomfort, nursing effort, and false positive diagnoses, together with a significant financial and environmental health care burden.[1,2,4-8] Choosing Wisely has identified targeted diagnostic testing as a high priority recommendation within ICUs.[5] Coagulation abnormalities in ICU patients may be related to medications (eg, anticoagulants, antiplatelets) or an underlying pathological process (ie, blood loss, sepsis, liver failure). It is unknown what proportion of ICU patients with an initial normal coagulation profile develops an abnormal coagulation profile.

To investigate the proportion of patients admitted to the ICU with a normal coagulation profile who went on to develop an abnormal coagulation profile, we interrogated an administrative dataset to retrospectively identify 500 consecutive patients with an initial normal coagulation profile admitted to two metropolitan ICUs. Our primary outcome was to describe the proportion of patients who developed an abnormal coagulation test. We also sought to describe the time to abnormal test and identify any risk factors that increase the likelihood of an abnormal test. A coagulation profile was defined as all of the following tests: prothrombin time, international normalised ratio (INR), activated partial thromboplastic time (aPTT), and fibrinogen (routinely ordered as a set at our health service). In our laboratory, a normal coagulation profile is an INR < 1.5 and aPTT < 40 seconds.

The study was performed in a metropolitan Victorian health service with 18 mixed tertiary ICU-equivalent beds across two campuses. The clotting profiles were performed routinely at 4:00–06:00 daily, and more frequently if there was clinical concern. No changes have occurred to pathology testing as of July 2021, and no ICU point-of-care clotting profiles were undertaken. Study approval was obtained at our institution (WH QA2018.32), with a waiver of consent.

Data extracted from the IntelliSpace Critical Care and Anaesthesia (ICCA) (Philips, Amsterdam, the Netherlands) information system included demographic data, Acute Physiology and Chronic Health Evaluation (APACHE) III scores and diagnosis, ICU and hospital length of stay, coagulation profile results (until ICU discharge or day 7 if the patient remained in the ICU), patient comorbidities, prescription of blood products or vitamin K, and administration of anticoagulants or antiplatelet agents. The included patients were admitted from 1 January to 6 June 2017. We excluded patients who did not have a coagulation profile performed within 6 hours of ICU admission, as our research aimed to determine the trend of coagulation parameters for patients who had normal coagulation on ICU arrival. Patients with multiple ICU admissions during the study period had their initial admission included, but subsequent admissions were excluded to prevent capturing data from patients transferred between campuses who had treatment already initiated. Patients who were prescribed therapeutic anticoagulation during their ICU admission were excluded.

Data were analysed using R 4.0.2 with the Survival and Survminer packages.[9] We performed descriptive statistical analyses, with data presented as mean with standard deviation (SD) and median with interquartile range (IQR). Categorical variables were compared using the χ^2 test (or Fischer exact test where the numbers were small), and continuous variables were compared with the Mann–Whitney U test. We calculated the duration from initially normal coagulation profiles to abnormal or to discharge. In addition, Kaplan–Meier analyses were performed to determine if there was a difference in the time taken for coagulation profiles to become abnormal in patients considered at higher risk for coagulation abnormalities. *A priori* we considered patients with a high risk of developing abnormal clotting profiles as those with an APACHE III diagnosis of sepsis, chronic liver disease, active bleeding, or a known coagulation disorder.

Of the 500 patients, 31 (6%) were prescribed therapeutic anticoagulant therapy during their ICU admission. Table 1 displays demographic data of the remaining 469 patients. Overall, the coagulation profile became abnormal in 61/469 ICU patients (13%). The mean ICU stay for patients whose coagulation became abnormal was 3.6 ± 3.0 days compared with 2.6 ± 3.3 days for patients whose coagulation remained

normal ($P < 0.001$). There were 134/469 patients (29%) at high risk of developing an abnormal coagulation profile. Of the 335 patients with a low risk of their coagulation becoming abnormal, 25/359 (7%) actually became abnormal compared with 36/134 patients (27%) for the high risk group ($P < 0.001$ for difference). For surgical patients, 19/131 (15%) had abnormal clotting profiles compared with 42/338 medical patients (12%; $P = 0.543$) (Table 1). For the surgical patients, 14/19 (74%) received gastrointestinal surgery.

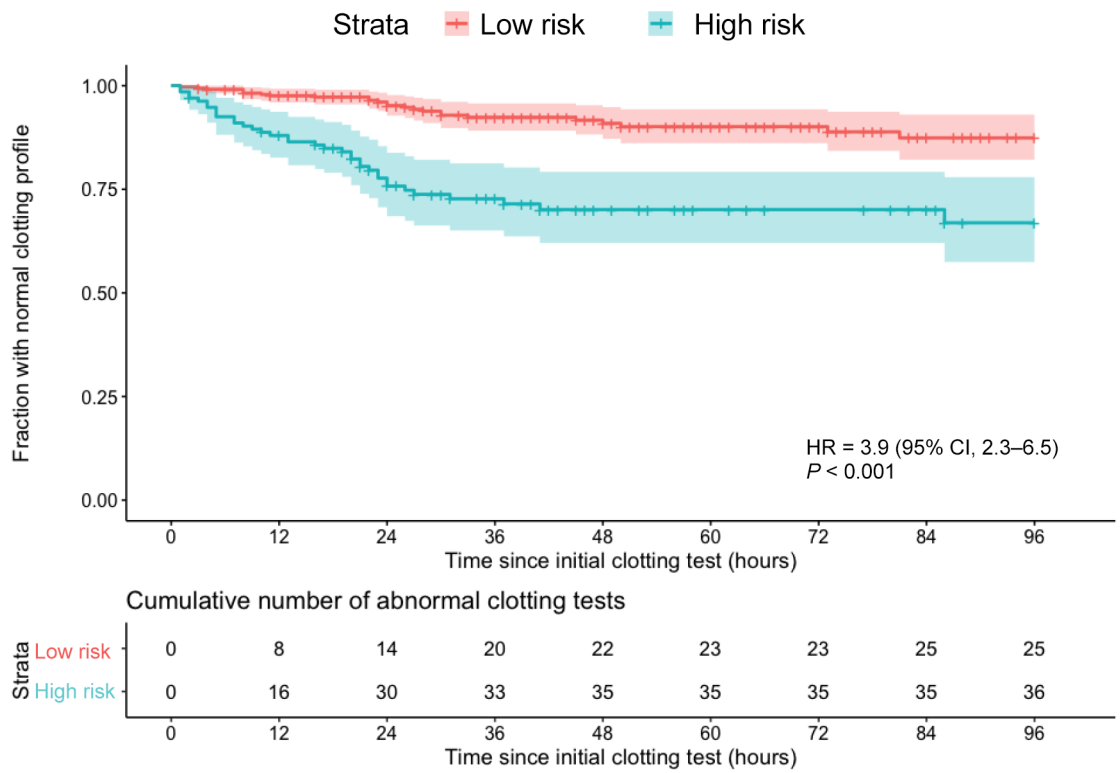
The median time for the clotting profile to become abnormal for all patients was 20 hours (interquartile range [IQR], 8–26 hours), for high risk patients was 14.5 hours (IQR, 5–23 hours), and for low risk patients was 24 hours

Table 1. Demographic details and results

Summary statistics	All patients	Coagulation became abnormal	Coagulation remained normal	*P*
Total number of patients	469	61/469 (13%)	408/469 (87%)	
Age, years, mean (SD)	58.3 ± 18.2	62.8 ± 16.8	57.6 ± 18.3	0.042
Sex				
Male	242 (52%)	35/61 (57%)	207/408 (51%)	0.341
Female	227 (48%)	26/61 (43%)	201/408 (49%)	
ICU LOS, days				
Mean (SD)	2.8 ± 3.3	3.6 ± 3.0	2.6 ± 3.3	< 0.001
Median (IQR)	2 (1.0–3.0)	3 (2.0–5.0)	2.0 (1.0–3.0)	
Admitting diagnosis				
Medical	338/469 (72%)	42/61 (69%)	296/408 (73%)	0.543
Surgical	131/469 (28%)	19/61 (31%)	112/408 (27%)	
Mortality	51 (11%)	10 (16%)	41 (10%)	0.182
APACHE III score, mean (SD)	69.0 ± 27.1	79.4 ± 27.3	67.5 ± 26.7	0.002
High risk of bleeding*	134/469 (29%)	36/61 (59%)	98/408 (24%)	< 0.001
Low risk of bleeding	335/469 (71%)	25/61 (41%)	310/408 (76%)	
Sepsis	74/469 (16%)	26/61 (43%)	48/408 (12%)	< 0.001
Chronic liver disease	19/469 (4%)	2/61 (3%)	17/408 (4%)	1
Bleeding	49/469 (10%)	9/61 (15%)	40/408 (10%)	0.26
Known coagulation disorder	1/469 (0%)	1/61 (2%)	0/408 (0%)	0.13
Received blood products†	6/469 (1%)	4/61 (7%)	2/408 (0%)	0.003
Received vitamin K	1/469 (0%)	1/61 (2%)	0/408 (0%)	0.145
Receiving antiplatelet‡ or anticoagulant§ therapy	139/469 (30%)	22/61 (36%)	117/408 (29%)	0.234
Multiple coagulation tests/day¶	125/469 (27%)	35/61 (57%)	90/408 (22%)	< 0.001
INR = 1.5–1.9	37/469 (8%)	37/61 (61%)	0/408 (0%)	< 0.001
INR ≥ 2	1/469 (0%)	1/61 (2%)	0/408 (0%)	< 0.001
APTT = 40–48	36/469 (8%)	36/61 (59%)	0/408 (0%)	< 0.001
APTT > 48	3/469 (1%)	3/61 (5%)	0/408 (0%)	< 0.001

APACHE = Acute Physiology and Chronic Health Evaluation; aPTT = activated partial thromboplastic time; ICU = intensive care unit; INR = international normalised ratio; IQR = interquartile range; LOS = length of stay; SD = standard deviation. * Patients could have more than one of the four risk factors for a high risk of bleeding; therefore, the addition of the four subgroups is greater than the total for both the patient groups (clotting profiles becoming abnormal and those remaining normal). † Products = clotting products, fresh frozen plasma, or cryoprecipitate. ‡ Antiplatelet therapy includes oral and intravenous antiplatelet drugs. § Anticoagulant therapy includes direct oral anticoagulants. ¶ Tests could be done on any ICU day.

Figure 1. Kaplan–Meier curve: time to abnormality of coagulation profile



HR = hazard ratio. High risk refers to sepsis, chronic liver disease, bleeding, or known coagulation disorder. For improved interpretability, survival times beyond 96 hours were truncated to 96 hours.

(IQR, 10–30 hours) (P = 0.03). Figure 1 shows the Kaplan–Meyer survival curve of patients whose clotting profile became abnormal over time. Patients considered high risk had a higher hazard ratio (HR, 3.9; 95% CI, 2.3–6.5) of abnormal clotting results, resulting in more of their clotting profiles becoming abnormal at an earlier time point (P < 0.001). Multiple clotting tests were performed per day in 125/469 patients (27%). Thirty-five of 61 patients (57%) who developed an abnormal coagulation profile had multiple tests per day compared with 90/408 patients (22%) whose coagulation profile remained normal. There was a statistically significant greater proportion of multiple tests per day for patients whose coagulation became abnormal (P < 0.001), suggesting more frequent testing due to clinical concern for these patients.

Most of the ICU patients whose clotting profile became abnormal did so within the first 48 hours of admission (Figure 1). Only four out of 61 patients (7%) whose clotting profile became abnormal did so after the first 48 hours. The abnormal clotting results after 48 hours were: INRs of 1.5 and 1.7 and aPTTs of 41 and 42. Beyond 86 hours (about 3.5 days), no clotting results became abnormal.

For patients with abnormal clotting profiles, four out of 61 (7%) received blood products, and one out of 61 (2%) received vitamin K (Table 1). The proportion of patients who received blood products was greater for patients with abnormal versus normal clotting profiles (P = 0.003).

In this retrospective study, only 13% (61/469) of patients admitted to the ICU with an initially normal coagulation profile went on to develop an abnormal coagulation profile during their ICU stay. In the majority of patients who developed an abnormal result, this occurred within the first 48 hours of ICU admission.

Our findings suggest that, for most ICU patients with normal coagulation on admission, further routine testing is of little clinical value. In the subset of patients with acute bleeding, sepsis, liver disease, or a known coagulation disorder on admission and normal coagulation at 48 hours, additional routine testing beyond this time point is of limited clinical value.

The practice of overtesting is well recognised within ICUs.[3] Research suggests that implementation of guidelines and changes in practice may result in reduced ordering, with no impact on patient outcomes (ICU or hospital length of stay, ICU or hospital mortality).[3] Decreasing the frequency of testing of clotting profiles can reduce the financial burden on health care systems and may increase the efficiency of hospital-based pathology services.[1,10,11]

This retrospective single health care centre (two ICUs) study has limitations: the hospitals do not have multitrauma, cardiothoracic or neurosurgical patients; therefore, the results may not be generalisable. We used an initial convenience sample of 500 patients, and excluded those receiving warfarin or heparin. Our ICU routinely tests coagulation profiles daily, in keeping with other studies demonstrating routine coagulation testing occurs in other Australian ICU settings, although we recognise this practice may differ between health services.[1,3] Future studies could consider interventions for more targeted tests; for example, having the test frequency vary by patient factors to identify the patients most at risk of having an abnormal clotting profile and involving relevant stakeholders for optimal intervention effectiveness.

We demonstrate that, for most patients admitted to the ICU with initially normal coagulation profiles, their coagulation remains normal through their ICU stay. If routine daily clotting tests were restricted to a total maximum of 3 days unless they became abnormal, coagulation testing may be reduced by nearly one-quarter. Our data could inform future prospective ICU studies to safely reduce unnecessary testing of clotting profiles.[12]

Competing interests

No relevant disclosures.

Author details

Forbes McGain[1,2]
Madeline Corke[1]
Fabien Dade[1]
Riley Hazard[1]
Dominique Grant[1]
Craig French[1,2,3]

1 Western Health, Melbourne, VIC, Australia.
2 Department of Critical Care, University of Melbourne, Melbourne, VIC, Australia.
3 Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia.

***Correspondence*:** forbes.mcgain@wh.org.au
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