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Letter to the Editor

LETTER TO THE EDITOR

Vaccination against COVID-19 in a haemodialysis centre: what is the risk of bleeding complications?

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The coronavirus disease 2019 (COVID-19) has become pandemic all around the World since its beginning in Wuhan in December 2019. Dialysis patients have a 20–30% risk of death in case of COVID-19 [1–3]. Recently, the Comirnaty vaccine (BNT162b2; BioNTech and Pfizer) has been developed and approved in Europe [4]. To protect dialysis patients from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), international guidelines recommend vaccinating dialysis patients [5, 6]. Dialysis patients have higher bleeding risk compared with the general population due to their uraemic status [7] and the frequent use of oral anticoagulants (OAC) [8] and/or antiplatelet agents [9]. This bleeding risk could be further increased during the dialysis session due to the anticoagulation of the extra corporeal circuit. The intramuscular vaccination in dialysis patients needs a safety evaluation. We performed vaccination on 10 and 11 February 2021 in every patient who gave their written consent in our haemodialysis centres. We analysed the bleeding complications after the first dose of Comirnaty vaccine in the deltoid muscle in a prospective manner.

Inclusion criteria were haemodialysis patients who accepted and received vaccination on 10 and 11 February 2021. Exclusion criteria were age <18 years, active or recent COVID-19 in the previous 3 months. Vaccination was done with the Comirnaty vaccine in deltoid muscle on the contralateral arm of arteriovenous fistula when present (see Supplementary data, Method).

Ninety dialysis patients were vaccinated against COVID-19. Two (2.2%) patients had the injection before the dialysis session, 27 (30%) in the two first hours of dialysis and 61 (67.8%) in the two last hours of dialysis. Timing of vaccination was not associated with bleeding complications (see Supplementary data, Figure S1). Twenty-three (25.5%) patients were treated with OAC. Among them, two patients taking apixaban skipped the dose the day before and on the day of the vaccine, and 21 patients used vitamin K antagonists (VKAs). Five (5.6%) patients continued VKA treatment for the following reasons: cardiac mechanic valve ($n=2$), antiphospholipid syndrome ($n=2$) and recent diagnostic of deep venous thrombosis ($n=1$). For the 16 remaining patients, VKA were managed at the physician's discretion. Eight patients skipped the doses the session before and on the day of the vaccine , four patients skipped the dose only at the previous session before the day of the vaccine and four patients skipped the dose only on the day of the vaccine . The international normalized ratio (INR) was lower than 3.2 for all the patients, on the vaccine day. Seventy-nine patients received unfractionated heparin during the dialysis sessions and two patients with history of heparin-induced thrombocytopenia received danaparoid sodium. The nine remaining patients did not receive anticoagulation during the dialysis session for the following reasons: two because OAC is usually sufficient to perform a 4-h dialysis session and seven had anticoagulation contraindication (two with cholesterol embolism disease and five with high bleeding risk).

Injection site was the contralateral shoulder at the vascular access. Age, history of COVID-19, use of antiplatelet agent, presence of thrombocytopenia and heparin dose did not differ according to anticoagulation status (see Supplementary data,

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Table S1). History of bleeding did not differ in the OAC group compared with the no OAC group (60.9 ± 10% versus 40 ± 6.1%, respectively, P = 0.09). No complications were reported on the day of the vaccine. At the next dialysis session, 48 h after the vaccine day, bleeding complications occurred in six (6.7%) patients, five (5.6%) with ecchymosis and one patient had both ecchymosis and deep haematoma <1 cm. OAC was not associated with bleeding complications (8.7 ± 2.9% in OAC versus 6.0 ± 2.4% in no OAC group, P = 0.64) (Figure 1A). INR >2 on the vaccine day was not associated with bleeding complications (20.0 ± 21.0% with INR >2 versus 6.7 ± 6.5% with INR <2, P = 0.39) (Figure 1B). Use of anticoagulant during the dialysis session was not statistically associated with bleeding complications (7.6 ± 3.0% versus 0%, P = 0.34) (Figure 1C). Use of antiplatelet agent or OAC alone, or both antiplatelet agent and OAC, were not associated with bleeding complications compared with using neither antiplatelet nor OAC (Figure 1D). The non-bleeding complications were as follow: mild-to-moderate pain at the injection site (*n* = 32; 35.6%) with one (1.1%) episode of redness and swelling; and systemic events including asthenia (*n* = 13; 14.4%), headache (*n* = 2; 2.2%) and flu syndrome with or without fever (*n* = 11; 12.2%) (see Supplementary data, Table S2). Interestingly, history of COVID-19 was associated with fever compared with no medical history of COVID-19 (18.2 ± 12% versus 2.5 ± 1.8%, respectively, P = 0.02). OAC treatment was associated with fewer events of flu syndrome (16.4 ± 4.6% versus 0%, P = 0.04) (see Supplementary data, Table S2).

Previous studies [10, 11] have shown the safety of intramuscular vaccine in patients receiving oral anticoagulation in the general population. In our study, only six minor bleedings complications occurred. OAC or heparin use was not associated with a significant risk of bleeding complications. Compared with the general population [4], dialysis patients may have fewer local and systemic events.

To ascertain that the vaccine is safe in the dialysis population under anticoagulation treatment, the number of subjects *a posteriori* to demonstrate the non-inferiority compared with the general population [4] is estimated at 23 944 under the following hypotheses: (i) a rate of serious adverse events in the general population of 1.1%, (ii) a non-inferiority margin of 0.2%, (iii) a one-sided alpha risk at 2.5% and (iv) a power of 80% [12–14]. The number of subjects needed makes this study difficult to

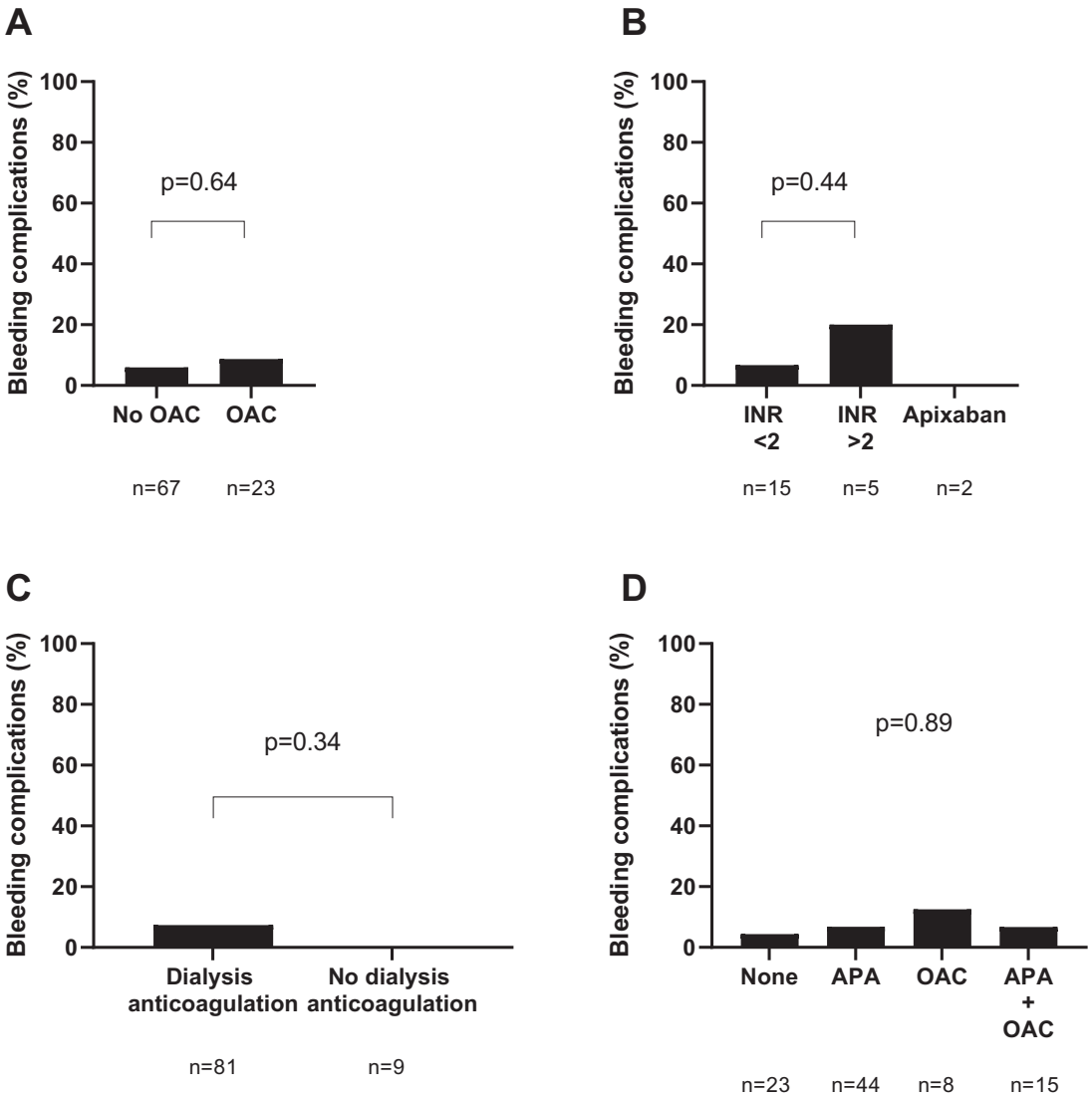

FIGURE 1: Risk of bleeding complications according to: OAC status (**A**), INR (**B**), dialysis session anticoagulation (**C**), antiplatelet agent and/or OAC use (**D**). APA, antiplatelet agent.

perform. However, vaccination seems safe in our cohort and the expected benefits far outweigh the observed risks.

To our knowledge, we are the first to study the safety of intramuscular vaccine concerning bleeding complications in chronic dialysis patients with OAC and/or heparin during dialysis session. In conclusion, vaccination against COVID-19 during the dialysis session appears to be safe, particularly regarding bleeding risk, even in patients under OAC.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

SUPPLEMENTARY DATA

Supplementary data are available at ckj online.

FUNDING

No funding was obtained for this study.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

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