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Endocavitary electrophysiological study by percutaneous antecubital vein and without X-ray for risk stratification of asymptomatic ventricular pre-excitation in young athletes

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ABSTRACT

Background: Athletes with asymptomatic ventricular pre-excitation (VP) should undergo electrophysiological study for risk stratification. We aimed to evaluate the feasibility, efficacy, safety and tolerability of an electrophysiological study using a percutaneous antecubital vein access and without the use of X-ray (ESnoXr). **Methods**: We collected data from all young athletes < 18 year-old with AVP, who underwent ESnoXr from January 2000 to September 2020 for evaluation of accessory pathway refractoriness and arrhythmia inducibility using an antecubital percutaneous venous access. Endocavitary signals were used to advance the catheter in the right atrium and ventricle. **Results:** We included 63 consecutive young athletes (mean age 14.6 ± 1.9 years, 46% male). Feasibility of the ESnoXr technique was 87% while in 13% fluoroscopy and/or a femoral approach were needed. Specifically, fluoroscopy was used in 7 cases to position the catheter inside the heart cavities with an average exposure of 43 ± 38 s while in 2 femoral venous access was needed. The mean procedural time was 35 ± 11 min. The exam was diagnostic in all patients, there were no procedural complications and tolerability was excellent. 53% of the patients had an accessory pathway with high refractoriness and no inducible atrioventricular reentry tachycardia: this subgroup was considered eligible to competitive sports and no event was observed during long-term follow-up (13.6 ± 5.2 years) without drug use. The others underwent catheter ablation. **Conclusion**. ESnoXr has been shown to be a feasible, effective, safe and well-tolerated procedure for the assessment of arrhythmic risk in a population of young athletes with asymptomatic VP.

1. Introduction

Wolff-Parkinson-White (WPW) syndrome accounts for at least 1% of deaths in a long-term registry of sudden cardiac death (SCD) in athletes [1]. Half of athletes with ventricular pre-excitation (VP) and SCD were asymptomatic before the event [2]. Several prospective studies have found that the risk of SCD in subjects with asymptomatic ventricular VP ranges from 0.1% to 0.45% per year [3–6].

For asymptomatic athletes with overt VP pattern on ECG persisting during exercise, the 2019 European Society of Cardiology guidelines on the management of supraventricular arrhythmias [7], as well as the Italian guidelines on eligibility to sports activity [8], recommend performing an electrophysiological study (EPS). The EPS carried out via the transesophageal route or via intracardiac catheterization proved to be effective in evaluating the characteristics of the accessory pathway (AP) [9]. The protocols for both transesophageal and intracardiac studies using the femoral approach are well described and the electrophysiological characteristics of the AP evaluated with the two techniques correlate well [10,11]. However, both methods have limitations: the transesophageal is characterized by poor tolerability and lower feasibility, while the traditional intracavitary approach is invasive, requires a full electrophysiological laboratory and exposes young patients to X-rays that could be harmful [12]. Another possibility is to carry out the EPS with non-fluoroscopic mapping systems but this increases the procedural costs.

The purpose of this work was to evaluate the results in terms of feasibility, efficacy, safety and tolerability of a third alternative which we have used in our center since 2000 for evaluation of the

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asymptomatic AP characteristics in young athletes referred for risk stratification: to perform the EPS using a percutaneous antecubital venous access and to advance a single catheter without the use of fluoroscopy and with the sole aid of endocavitary registration (ESnoXr). We also evaluated the outcome of ESnoXr, the locations of the AP and the follow-up of patients undergoing this method.

2. Methods

We collected the data of all young athletes (<18 year-old) with asymptomatic VP persistent on the stress test and normal echocardiogram, who underwent ESnoXr from January 2000 to September 2020 for risk stratification and decision on eligibility to competitive sports activity.

2.1. ESnoXr methodology

The ESnoXr approach consists of a right or left percutaneous antecubital right cardiac catheterization without the use of fluoroscopy but by positioning the catheter in the right cardiac cavities with only the reference of the intracardiac electrical signal.

The skin is disinfected, a sterile field is set up and, after local anesthesia with mepivacaine at 1% 2–3 cc, either the right basilic vein a few centimeters above the elbow crease or the intermediate (median) cubital vein is cannulated using the Seldinger technique; as a second choice, the cephalic vein is used, always at the level of the elbow (Fig. 1). This venous route is preferable to the jugular, subclavian or femoral route due to the lower risk of complications.

A Cordis pediatric 4 french (fr) introducer with 0.21 in. guide and a 4 fr Bard 4-pole catheter with 2–5-2 spacing (Fig. 1) or alternatively a Cordis pediatric 5 fr introducer with 0.38 in. guide and a Torqr (Medtronic) 5 Fr tetrapolar catheter with 5–5–5 spacing is inserted. The catheters are intentionally pushed into the vein without the use of fluoroscopy up to the atrium and subsequently into the right ventricle, as demonstrated by the recording of the endocavitary signals through the catheter (Fig. 2). When difficulties are encountered in advancing the catheter due to the presence of a valve, the patient is asked to perform a Valsalva maneuver or a saline bolus is quickly injected from the venous introducer to open the valve and advance the catheter.

The EPS steps are the following:

- the catheter is initially positioned in the ventricle to evaluate the retrograde conduction (to the surface ECG) and the possible induction of atrio-ventricular reentry tachycardia (AVRT) through a programmed stimulation with 1 and 2 extra stimuli (Fig. 3);
- the catheter is then withdrawn into the atrium and the refractory periods of the AP and atrio-ventricular node are evaluated by means of programmed atrial stimulation (Fig. 4) and subsequently by incremental stimulation (up to the refractoriness of the AP and to the Wenckebach point of the atrio-ventricular node);
- atrial bursts are then delivered up to 200 ms per cycle to induce atrial fibrillation and the possible percentage of pre-excited beats and the minimum R-R interval during pre-excited atrial fibrillation are measured;
- if the effective refractory period of the AP isis greater than 250 ms at baseline, all these evaluations are repeated also during the infusion of isoproterenol. Isoproterenol is initially infused at 4 mg/min until a stable increase of 50% of the basic heart rate is obtained; thereafter, the infusion rate is maintained or reduced to 1 mg/min as required to steadily maintain the 50% increase in baseline heart rate.

All patients were not taking antiarrhythmic therapy at the time of the study. For the procedures we used a Bard Lab System Duo polygraph with EP2 - Digital Cardiovascular Instruments stimulator.

2.2. End-point of the study

We evaluated the feasibility, efficacy, safety and tolerability of ESnoXr for the assessment of arrhythmic risk in young athletes with AP. We also evaluated the location of the APs and the follow-up of patients undergoing this procedure.

The feasibility was defined by the percentage of patients in which the study was able to be completed by percutaneous antecubital route without the use of fluoroscopy. Effectiveness is the ability to produce the desired or hoped-for effect results and in this case the measure of effectiveness was expressed as the percentage of patients in which the method allowed to formulate the diagnosis (presence and refractoriness of the AP) with respect to the total number of patients. Safety was assessed on the basis of the number and type of complications. Tolerability was assessed using a questionnaire on a scale of 1 to 10 administered to the patient at the end of the procedure (1 = poor tolerance – 10 = excellent tolerance).

This study complies with the Declaration of Helsinki on Human Research and all patients signed informed consent to the procedure. The Ethical Committee approved the study as an observational and retrospective investigation.

2.3. Statistical analysis

Continuous measures were expressed as mean and standard deviation, while categorical variables as absolute value and percentage. Data were analyzed with Microsoft Excel, Microsoft Corp, USA.

3. Results

The study population included 63 young athletes (mean age 14.6 ± 1.9 years, 46 males) with asymptomatic VP, persistent on the stress test, who underwent ESnoXr from January 2000 to September 2020 for

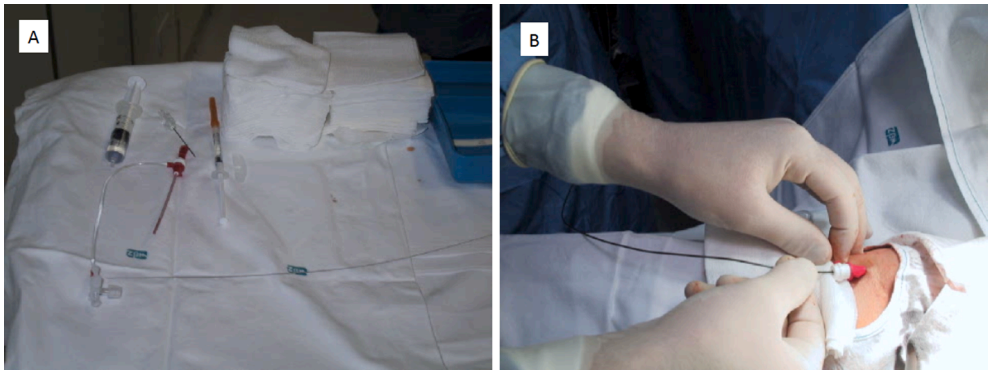

Fig. 1. Materials needed for ESnoXr. A) syringe with physiological solution, 4 French pediatric Cordis introducer, needle for brachial puncture, 0.21 in. guide, local anesthesia in insulin syringe; B) 4 fr Bard tetrapolar catheter which is introduced percutaneously in the antecubital vein.

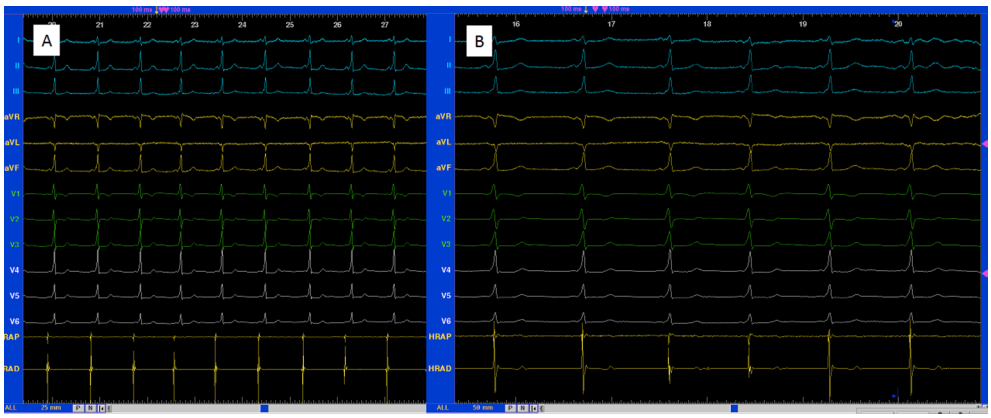

Fig. 2. A) catheter positioned in the atrium, records the atrial signal; B) catheter positioned in the right ventricle guided by the recording of the endocavitary signal.

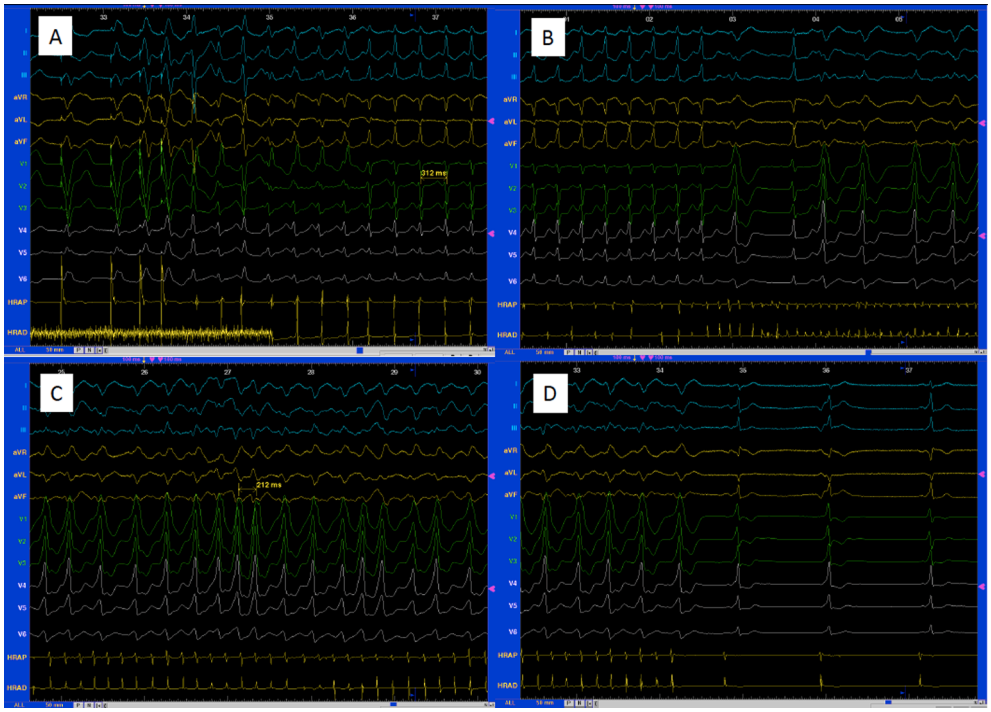

Fig. 3. A) programmed pacing from the right ventricle with induction of orthodromic atrioventricular reentry tachycardia; B) catheter withdrawn into the atrium and degeneration of the tachycardia into pre-excited atrial fibrillation; C) minimum RR during pre-excited atrial fibrillation 212 ms, indicative of high-risk accessory pathway; D) spontaneous restoration of sinus rhythm.

evaluation of AP characteristics and eligibility to competitive sport.

3.1. Feasibility, efficacy, safety and tolerability of ESnoXr

ESnoXr was performed with the use of a percutaneous antecubital venous access and without the use of fluoroscopy in 55 (87%) patients while in 8 (13%) fluoroscopy and/or the femoral approach were needed.

In particular, in 7 cases it was necessary to use fluoroscopy to position the catheter inside the heart cavities, in such cases the average use of fluoroscopy was 43 ± 38 s. All procedures with radiological exposure occurred in the first 32 cases performed, in the following 31 no ionizing radiation was used for the placement of the catheter in the right heart chambers. The mean procedural time was 35 ± 11 min, divided as follows: 1.6 ± 0.9 min to cannulate the vein, 5.4 ± 5.3 min to place the catheter and 28.3 ± 6.8 min for the electrophysiological study.

The study was carried out via the brachial route in 61 of the 63 patients: in 55 the catheter was positioned in the right heart via the right basilic or antecubital vein and in 6 cases using the left basilic after failure of the right arm approach. In 2 patients both approaches failed and a traditional right femoral approach was needed (Fig. 5).

The effectiveness was 100%: a diagnostic response was obtained with this method in all patients. Safety was excellent: there were no procedural or periprocedural complications. Compliance with the ESnoXr approach was evaluated using a questionnaire in 31 patients: the mean tolerability score (expressed on a scale from 1 = poorly tolerated to 10 = well tolerated) was 8.1 ± 1.4.

3.2. Electrophysiological evaluation

The results of the electrophysiological study are shown in Fig. 6. In three subjects with antero-septal VP appearance, fasciculoventricular fibers were diagnosed and no arrhythmias were induced. Atrial fibrillation was induced in 36 cases. Thirty-two (53%) of 60 patients with atrioventricular AP had a refractory period > 250 ms at baseline, >200

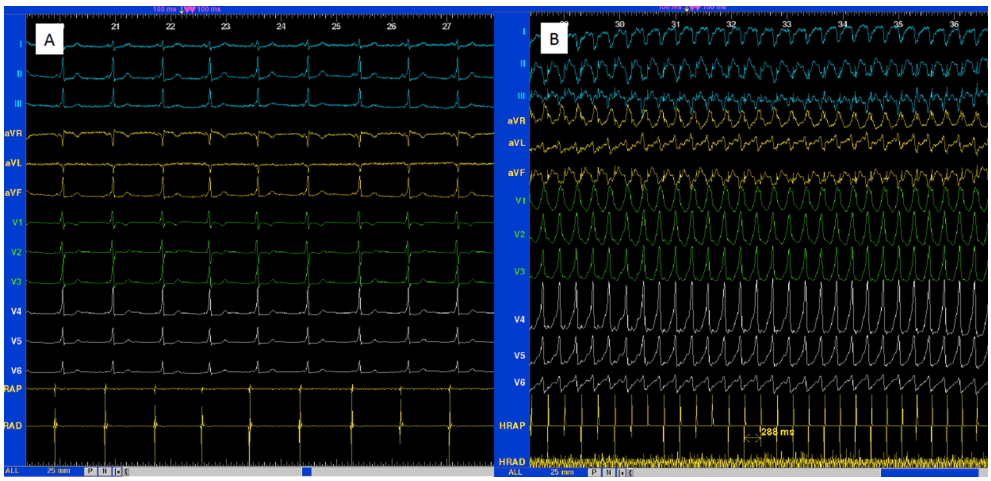

Fig. 4. A) four-pole catheter positioned in the atrium; B) incremental pacing to increase the degree of ventricular pre-excitation.

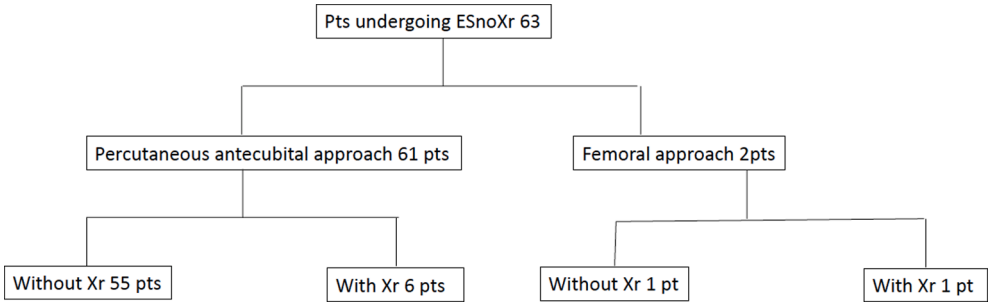

Fig. 5. Venous access used to perform ESnoXr. pt = patient, pts = patients, Xr = radiological exposure.

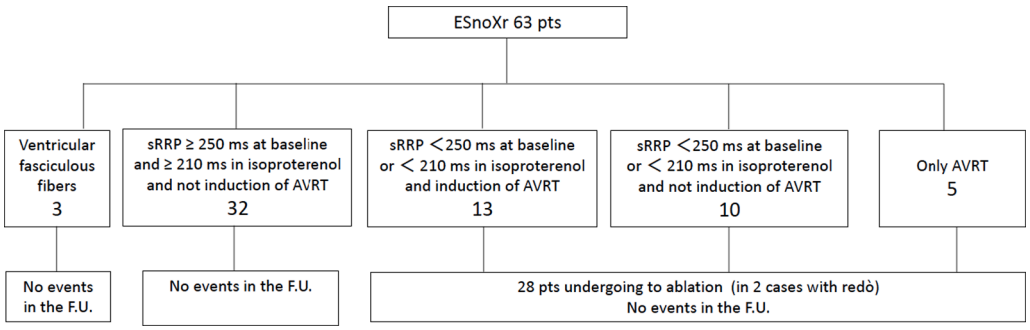

Fig. 6. ESnoXr results. AVRT = atrioventricular reciprocating tachycardia; F.U. = follow-up; ESnoXr. endocavitary electrophysiological study by percutaneous antecubital approach without use of fluoroscopy and with the aid of endocavitary recording; sRRP = the shortest RR interval between two pre-excited QRS.

ms during isoproterenol infusion and no inducible AVRT. These patients were considered eligible to competitive sports activity and no events were observed during long-term follow-up (13.6 ± 5.2 years) without drugs. In contrast, the remaining 28 patients (47%) met at least one criterion for ablation: 82% (23 of 28) had rapid antegrade conduction on the AP and 64% (18 of 28) had at least one AVRT inducible (orthodromic in 17 patients and antidromic in 1).

3.3. Locations of the accessory pathways

The predicted locations of the APs assessed on the surface ECG during maximum pre-excitation [13] were: antero-septal in 2 patients, mid-septal in 4, right postero-septal in 9, left postero-septal in 8, left posterior in 4, left posterolateral in 9, left lateral in 19 and left antero-lateral in 5 patients (Fig. 7).

4. Discussion

ESnoXr has been shown to be a feasible, effective, safe and well tolerated procedure for risk assessment in a population of young athletes (10–18 year-old) with asymptomatic VP that persisted during stress testing referred for risk stratification and evaluation of competitive sport eligibility.

In literature we have found other studies that have evaluated the antecubital approach for right catheterization, but to our knowledge this is the first that applies the approach without X ray use and to perform an electrophysiological study [14–16].

This procedure could be carried out in a short time (35 ± 11 min) even in a basic electrophysiological environment. In 89% of cases it did not required the use of ionizing radiation while in the remaining 7 cases the radiological exposure was minimal. All the procedures with

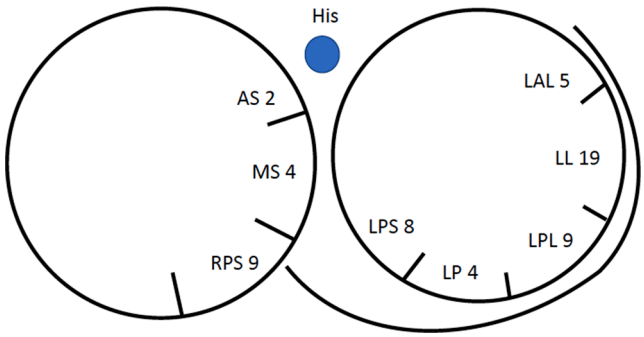

Fig. 7. locations of the anomalous pathways found at EsnoXr. AS = antero-septal; LAL = left anterolateral; LL = left lateral; LP = left posterior LPL = left posterolateral; LPS = left postero-septal; MS = mid-septal; RPS = right postero-septal.

radiological exposure occurred in the first 32 cases performed, in the following 31 no ionizing radiation was used for the positioning of the catheter in the right heart chambers, suggesting a learning curve. For example, when difficulties are encountered in advancing the catheter due to the presence of a valve, we learned to ask the patient to perform a Valsalva maneuver or to inject a saline bolus quickly from the venous introducer to open the valve and advance the catheter as suggested in methods.

In 61 out of 63 cases the catheter was advanced through the superficial veins of the elbow (basilic or cephalic). This route was chosen in such young individuals because of the higher tolerability and lower risk of complications compared to other possible accesses such as the jugular, subclavian and femoral routes. The mean tolerability of the procedure reported by patients was 8 out of 10.

The ESnoXr with infusion of isoproterenol as recommended by the Italian guidelines for eligibility to competitive sports [8] found that 32 out of 60 (53%) with a confirmed atrioventricular AP did not show electrophysiological high-risk features: this subgroup was considered eligible to competitive sports under annual surveillance (or earlier should arrhythmic symptoms develop) and no events were observed during long-term drug-free follow-up. The data is in line with previous experiences [17] and support the negative predictive value of the electrophysiological test.

The remaining cases showed rapid antegrade conduction on the AP (82%) and/or inducible AVRT (64%). Two previous studies [17,18] reported a similar percentage of high-risk APs characteristics in asymptomatic young subjects with overt VP that persisted on stress test. The AP refractory period was evaluated during atrial fibrillation in 40% of cases and in the remaining during rapid atrial pacing because atrial fibrillation was not inducible even during isoproterenol infusion. Although the evaluation of antegrade conduction on the AP during a prolonged episode of atrial fibrillation may be more indicative of what might happen clinically, refractoriness determined during rapid atrial pacing is considered a reasonable surrogate [19]. An ablative approach is recommended in patients with AP with low refractoriness or ARVT induction [8,19,20,21]. In accordance with these recommendations, subjects with high-risk AP underwent catheter ablation.

4.1. Study limitations

This is a single center study including a relatively small sample of patients collected over a long time period. For this reason, results particularly in terms of feasibility requires validation with further studies in different centers. Comparison with standard transvenous electrophysiological study or with transesophageal study was not possible because the ESnoXr has been the standard of care in our center for over 20 years. Another limitation of ESnoXr is that a second (traditional) procedure is require to perform catheter ablation in case an at-risk AP is detected.

5. Conclusions

ESnoXr has been shown to be a feasible, effective, safe and well tolerated procedure for arrhythmic risk assessment in a population of young athletes aged 10 to 18 years with asymptomatic VP. In fact, the ESnoXr technique allowed to evaluate the characteristics of the AP inserting the catheter in the elbow vein and without the use of X-rays in 83% of patients and mean tolerability was 8 out of 10. In more than half of patients, the AP was considered at low-risk and they were cleared to competitive sports, demonstrating an excellent long-term follow-up. For these reasons, the ESnoXr procedure may be considered a safe, less invasive and better tolerated alternatives to the traditional *trans*-esophageal or *trans*-femoral approaches.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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