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How many atrial fibrillation ablation candidates have an underlying supraventricular tachycardia previously unknown? Efficacy of isolated triggering arrhythmia ablation

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Aims Supraventricular tachycardia may trigger atrial fibrillation (AF). The aim of the study was to evaluate the prevalence of supraventricular tachycardia (SVT) inducibility in patients referred for AF ablation and to evaluate the effects of SVT ablation on AF recurrences.

Methods and results Two hundred and fifty-seven patients (185 males; mean age: 53.4 ± 14.6 years) referred for AF ablation were studied. In all patients only AF relapses had been documented in the clinical history. Twenty-six patients (10.1%; mean age: 43.4 ± 13.3 years; 17 males) had inducible SVT during electrophysiological study and underwent an ablation targeted only at SVT suppression. Ablation was successful in all 26 patients. The ablative procedures are: 12 slow-pathway ablations for atrioventricular nodal re-entrant tachycardia; 9 concealed accessory pathway ablations for atrioventricular re-entrant tachycardia; and 5 focal ectopic atrial tachycardia ablations. No recurrences of SVT were observed during the follow-up (21 ± 11 months). Two patients (7.7%) showed recurrence of at least one episode of AF. Patients with inducible SVT had less structural heart disease and were younger than those without inducible SVT (interventricular septum thickness: 8.4 ± 1.6 vs. 11.0 ± 1.4 mm, $P < 0.01$; left atrial diameter: 37.0 ± 3.0 vs. 44.0 ± 2.2 mm, $P < 0.01$; age: 43.4 ± 13.3 vs. 57.3 ± 11.2 years, $P < 0.01$). Prevalence of paroxysmal AF was higher in patients with inducible SVT when compared with those with only AF (84.6 vs. 24.6%, $P < 0.01$).

Conclusion A significant proportion of candidates to AF ablation are inducible for a SVT. SVT ablation showed a preventive effect on AF recurrences. Those patients should be selected for simpler ablation procedures tailored only on the triggering arrhythmia suppression.

Keywords Atrial fibrillation • Supraventricular tachycardia • Ablation

Introduction

Transcatheter ablation focused on trigger suppression is known to be an effective strategy to cure patients affected by atrial fibrillation (AF).[1–3] It is well known that the most common sites of ectopic beats that trigger AF are situated in or around the pulmonary veins ostia.[1,4] However, also supraventricular tachycardias (SVTs), such as atrioventricular nodal re-entrant tachycardia (AVNRT), atrioventricular re-entrant tachycardia (AVRT) through an accessory pathway, focal atrial ectopic tachycardia (FAT) and typical atrial flutter can be associated with AF.[5–14] It has been reported that SVT ablation may prevent recurrences of AF in patients with documentation of both arrhythmias.[5–7,10,13,14] Moreover, some AF ablation candidates may have un underlying SVT discovered at

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the electrophysiological study, and it has been observed that ablation of a SVT in adjunction to pulmonary veins ablation can be an ideal treatment in such patients.[8,9] However, to date only few data are available about the effects of ablative strategy focused only on the elimination of the triggering arrhythmia, discovered at electrophysiological study in AF ablation candidates.[8,9] It is of clinical relevance that an ablation procedure focused on the SVT elimination may determine a reduction of recurrences of AF, particularly in young patients and in absence of structural heart disease.[5–14] The aim of our study was to evaluate the prevalence of SVT inducibility in patients referred for ablation of AF and to investigate on the effects of SVT ablation on AF recurrences.

Methods

Study population

Two hundred fifty-seven patients (185 males; mean age: 53.4 ± 14.6 years) were referred to our electrophysiology centre for catheter ablation of paroxysmal and/or persistent AF. Patients had to be highly symptomatic for recurrent sustained palpitations due to drug-resistant paroxysmal and/or persistent AF, and with important limitation of quality of life. All the AF ablation candidates had to be symptomatic for at least three episodes of sustained palpitations due to AF in the 6 months before ablation. Symptoms had been present for 3.2 ± 1.8 years before ablation. According to the international guidelines, AF was defined as paroxysmal when it was recurrent and self-terminating, and as persistent when sustained beyond 7 days.[15] All patients studied had been carefully investigated in order to exclude a history of suspected or documented SVT: in none of the patient a SVT history was present. Seventy-nine patients (30.7%) had paroxysmal AF and 178 patients (69.3%) paroxysmal and/or persistent AF. Among the 178 patients with persistent AF, 87 patients had both paroxysmal and persistent AF. Among this subgroup of patients, 17 subjects presented both clinical forms of the arrhythmia during all the clinical history, while, in the remaining 70 patients, a transition from paroxysmal to persistent AF was observed. The mean time for conversion from paroxysmal AF to persistent AF was 18 ± 8 months.

One hundred eighty-seven patients (72.8%) were affected by systemic hypertension (44.0% with hypertensive heart disease), 64 patients (24.9%) by coronary artery disease, 61 patients (23.7%) by hypercholesterolemia and 51 patients (19.8%) had not clinical and echocardiographic evidence of structural heart disease or cardiovascular risk factors.

In every patient an electrophysiological study (EPS) preceding the ablation procedure was planned. In order to concentrate our attention on patients without previously known AF triggers, patients affected by typical atrial flutter and manifest pre-excitation were excluded.

Electrophysiological study and ablation procedure

All patients underwent an EPS in order to identify those with an inducible SVT. Antiarrhythmic drugs were interrupted for at least five half-lives before the procedure. Amiodarone was stopped at least 1 month before EPS. All patients provided written informed consent prior to EPS and ablation. The procedure was performed with the patient in the fasting state using mild sedation and under local anaesthesia. If the patients were in AF an electrical cardioversion was performed in order to restore sinus rhythm. Up to three attempts of cardioversions were performed at a maximum energy of 200 J (biphasic shock): if AF relapsed after three shocks, no more attempts to obtain sinus rhythm were performed and the EPS was interrupted. No antiarrhythmic drug was infused during the EPS. Electrophysiological study was carried out according to standard protocols.[16] In brief right atrial and ventricular refractory periods at one or more cycle lengths were performed with decremental pacing. Programmed stimulation in the atrium and ventricle was performed. The electrophysiological assessment included the observation of dual atrioventricular nodal pathways, a significance prolongation of atrial-His bundle interval (jump) and a ventriculo-atrial time <70 ms during AVNRT and >70 ms during AVRT in association with eccentric atrial activation showed during the ventricular pacing.[16] Entrainment manoeuvres were performed to differentiate AVNRT from atrial tachycardia and AVRT. In the absence of tachycardia inducibility, a graded isoproterenol intravenous infusion (2–6–12 μg/min) was performed. Diagnostic criteria for FAT were considered: variability of VA intervals during tachycardia or ventricular pacing, ventricular-atrial-atrial-ventricular response before tachycardia resume during ventricular pacing, AH interval during atrial pacing at tachycardia cycle length minus AH interval during tachycardia ≤20 ms, spontaneous termination of tachycardia without an atrial activation.[16] Supraventricular tachycardia and AF were considered inducible if their duration was >1 min.

All patients with inducible SVT during EPS underwent an ablation procedure only aimed at the elimination of the SVT without any other extra radiofrequency lesion. Details about AVNRT and AVRT ablation procedure have been described elsewhere.[16–20] Focal atrial ectopic tachycardia ablation target sites were: atrial bipolar electrogram preceding P wave onset by at least 15–60 ms, monophasic negative unipolar recording, presence of early fractionated electrograms and earliest bipolar activation site identified by a 3D mapping system.[13,16,21–23] Left FATs ablation was performed by means of a *trans*-septal puncture, and an irrigated-tip quadripolar catheter with a distal 3.5-mm tip (42°C; 30 W) was used for mapping and RF application.

After the ablation procedures all the patients were continuously monitored for 36–48 h. A 12-lead surface ECG was obtained before hospital discharge.

Follow-up

In patients who underwent SVT ablation no antiarrhythmic drug was prescribed during follow-up. After the ablation procedure, a transtelephonic monitoring for 1 month was performed, with recordings taken twice daily and in case of appearance of any symptom. Transtelephonic ECG monitoring was also used subsequently, in case of recurrence of any symptom, at 6–8 weeks, and after 3 and 6 months. The follow-up included clinical evaluation, basal surface 12-lead ECG and 24-h Holter evaluation at 1, 3, 6 months after ablation and then every 6 months. In symptomatic patients, an extra visit was planned. Patients were instructed to call our outpatient ambulatory in case of symptoms. Even the first weeks after ablation were considered in the data collection. Any recurrence of SVT or AF was considered as a failure of ablative therapy.

Statistical analysis

Statistical analysis was performed using SPSS statistical software (version 15.00, Chicago, IL, USA). Continuous variables were presented as means ± SD and categorical values as frequencies (%). The association between categorical variables was evaluated using Fisher's exact test. Differences in continuous variables were determined for statistical significance by the use of independent samples of *t*-test or Mann–Whitney test. Statistical significance was defined as a two-sided probability value <0.05.

Results

Clinical characteristics of patients and comparison between patients with and without inducible supraventricular tachycardia

Twenty-six patients (10.1%; mean age: 43.4 ± 13.3 years; 17 males) had an inducible SVT during EPS (*Table 1*) and were treated with an ablation procedure targeted only at SVT elimination. In the study group of patients with SVT inducibility, prevalence of paroxysmal AF was 84.6%. Twenty patients (76.9%) of this group with AF and SVT had not clinical and echocardiographic evidence of structural heart disease; 6 patients (23.1%) were affected by systemic hypertension; one patient (3.8%) had coronary artery disease and one patient (3.8%) was affected by hypercholesterolemia.

Table 1 Characteristics of patients with or without inducible synchronized paroxysmal supraventricular tachycardia at electrophysiological study

	AF and inducible SVT ($n = 26$)	AF without inducible SVT ($n = 231$)	*P*-value
Age (years)	43.4 ± 13.3	57.3 ± 11.2	<0.01
Male gender, *n* (%)	17 (65.4)	168 (72.7)	NS
Type of AF, *n* (%)			
Paroxysmal	22 (84.6)	57 (24.6)	<0.01
Persistent	4 (15.4)	174 (75.4)	<0.01
Risk factors and heart disease aetiology, *n* (%)			
CAD	1 (3.8)	63 (27.2)	=0.02
Hypertension	6 (23.1)	181 (78.3)	<0.01
Hypercholesterolemia	1 (3.8)	60 (25.9)	=0.02
Absence of heart disease	20 (76.9)	31 (13.4)	<0.01
Echocardiography			
EF (%)	56.4 ± 6.1	54.2 ± 5.7	NS
Septal thickness (mm)	9.4 ± 1.6	11.0 ± 1.4	<0.01
Posterior wall thickness (mm)	9.9 ± 1.8	10.9 ± 1.3	<0.01
Left atrium AP diameter (mm)	37.0 ± 3.0	44.0 ± 2.2	<0.01
Therapy, *n* (%)			
Amiodarone	9 (34.6)	170 (75.6)	<0.01
Beta-blockers	4 (15.4)	125 (54.1)	<0.01
Sotalol	3 (11.5)	29 (12.5)	NS
Flecainide	5 (19.2)	91 (39.4)	NS
Propafenone	13 (50.0)	83 (35.9)	NS
Verapamil	4 (15.4)	25 (10.8)	NS
ACEi, ARB	2 (7.7)	190 (82.2)	<0.01
Statins	1 (3.8)	58 (23.1)	=0.04

ACEi, ACE inhibitors; AF, atrial fibrillation; AP, antero-posterior; ARB, angiotensin receptor blockers; CAD, coronary artery disease; EF, ejection fraction; NS, non-significant; SVT, supraventricular tachycardia.

Among candidates for AF ablation, patients treated with SVT ablation represented a significant younger population, when compared with patients without evidence of SVT inducibility during EPS and who had undergone AF transcatheter ablation through pulmonary veins encircling/deconnection (43.4 ± 13.3 vs. 57.3 ± 11.2 years; $P < 0.01$). Prevalence of paroxysmal AF was significantly higher in patients with inducible SVT when compared with those without (84.6 vs. 24.6%, $P < 0.01$). Moreover, patients without inducible SVT and treated with AF ablation, showed a higher prevalence of echocardiographic signs of structural heart disease, when compared with patients who had undergone SVT ablation (interventricular septum thickness: 11.0 ± 1.4 vs. 9.4 ± 1.6 mm, $P < 0.01$; posterior wall: 10.9 ± 1.3 vs. 9.9 ± 1.8 mm, $P < 0.01$; left atrial antero-posterior diameter: 44.0 ± 2.2 vs. 37.0 ± 3.0, $P<0.01$).

Electrophysiological study and ablation results

Inducibility of SVT was achieved in the basal condition in 14 patients (53.8%) and during isoproterenol infusion in 12 patients (46.2%). Transition from SVT into AF during EPS (*Figure 1*) was observed in 11 patients (42.3%). In 7 of those 11 subjects SVT inducibility had been achieved during isoproterenol infusion. In five patients (19.2%) with SVT inducibility we observed AF inducibility non-related to the SVT as well. However, even in such a subgroup of patients, the ablation strategy was similar to other subjects and was addressed only at the SVT elimination.

Ablation procedure was successful in all patients. No complication occurred. The mean procedural time was 78 ± 31 min and the mean fluoroscopy time was 16 ± 12 min. Twelve patients (46.2%) underwent slow-pathway ablation for AVNRT (11 of these were common slow-fast tachycardia and one was slow–slow tachycardia); 9 patients (34.6%) were ablated for a concealed accessory pathway with AVRT inducibility; 5 patients (19.2%) underwent ablation for FAT (2 left FATs).

Follow-up

After the ablation procedure, every patient was free from antiarrhythmic drug therapy. The mean follow-up duration of the study was 21 ± 11 months. Freedom from AF was achieved in 24 patients (92.3%) who had undergone SVT ablation. Moreover, no recurrence of SVT was documented. Two patients (7.7%; one with left-sided accessory pathway and one with FAT) showed a recurrence of at least one episode of paroxysmal AF. In one of these two patients, after oral propafenone administration, a significant improvement of symptoms was achieved, so pharmacological therapy was continued. In the other patient, symptomatic recurrences of paroxysmal and persistent AF occurred despite antiarrhythmic drug therapy (sotalol and propafenone), and the patient underwent AF ablation through pulmonary veins encircling/isolation. A flow chart of the study is presented in *Figure 2*.

Discussion

Major findings

Our study suggests that patients candidates to AF ablation and with inducibility of SVT during EPS represent a small but important

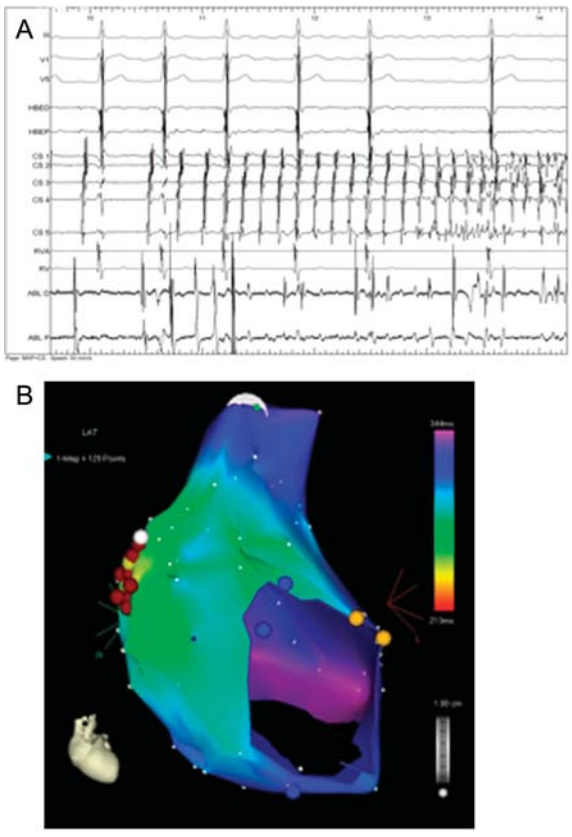

Figure 1 (*A*) The surface ECG recordings and intracavitary recordings show the transition from a right ectopic focal atrial tachycardia (first two beats) into atrial fibrillation. The tip of the ablative catheter is in the lateral medium right free wall. (*B*) The antero-posterior view of the right atrial electro-anatomical mapping during atrial tachycardia in the same patient. The red points are located in the effective site of radiofrequency application. III, V1, V5, surface ECG leads; HBED, distal bipolar His bundle electrogram; HBEP, proximal bipolar His bundle electrogram; CS 1–5, coronary sinus bipolar electrograms from distal to proximal; RVA, right ventricular apical bipolar electrogram; RV, right ventricular apical proximal bipolar electrogram; ABL D, mapping and ablator catheter distal bipolar electrogram; ABL P, right ventricular proximal apical bipolar electrogram.

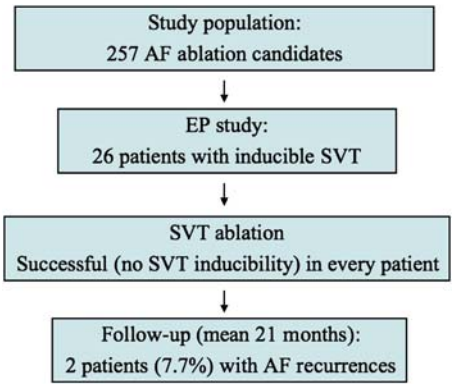

Figure 2 The figure represents a flow chart that summarizes the study design and the follow-up results. Abbreviations used are the same as in the text.

subgroup of AF patients. Such a population seems to be younger and with less structural heart disease when compared with the general population referred for AF ablation procedure in our laboratory. The EPS seems to have a crucial role to identify such a subgroup of subjects. In these patients, more simple and safer ablative strategy, tailored only on SVT suppression, resulted in a favourable follow-up with a very low incidence of AF recurrences, despite the absence of any antiarrhythmic therapy.

Atrial fibrillation ablation

Several studies support the concept that transcatheter ablation is an effective therapy to prevent AF recurrences.[2,3,24–34] Many ablative approaches have been focused on the principal electrophysiological mechanisms that can initiate and sustain AF.[1,35–38] Both trigger suppression and substrate modification have been proposed as appropriate targets to cure AF.[1,26–30] However, in the real world the price that we pay in terms of complications related to AF ablation does not seem to be insignificant. Cappato *et al.*,[39] in their recent worldwide survey, showed a 4.54% rate of major complications related to the AF ablation procedure. In order to improve the success rate and to optimize the benefit/risk ratio, some authors tried to investigate on the possibility to perform ablative procedure tailored on the electrophysiological mechanisms of the single patients. Oral *et al.*[40] showed a 77% of freedom from AF recurrences during a mean follow-up of 11 months, using a tailored ablation strategy only targeted on AF initiators and drivers elimination, in 153 patients affected by paroxysmal AF.

Non-pulmonary veins atrial fibrillation triggers

It is well known that the principal AF triggers are located in or around the pulmonary veins ostia.[1,27,28] Pulmonary veins are also known to play an important role in the maintenance and perpetuation of AF.[1,33,34] Furthermore, it has been observed that synchronized tachycardias such as atrial flutter, AVNRT, AVRT and FAT may trigger AF. In fact, AF frequently occurs in patients affected by Wolff-Parkinson-White (WPW) syndrome.[7–9] In patients affected by WPW syndrome, the accessory pathway is considered to be important for the development of AF and frequent tachycardias are known to promote an electrical remodelling that favours AF.[41] After successful ablation of the accessory pathway, the majority of patients are free from AF episodes in the follow-up.[41] Several studies have shown the potential role of AVNRT as an AF trigger.[5–9] It has been suggested that the fast atrial activation that occurs during AVNRT may degenerate into AF.[5] Moreover, it has been reported that the transition from AVNRT into AF may begin inside the pulmonary veins.[11] Brugada *et al.*[6] in a very small study conducted in four patients affected by paroxysmal AF and without evidence of structural heart disease, first described AVNRT inducibility at the EP study. The elimination of the

synchronized tachycardia resulted in the absence of both AVNRT and AF in the follow-up. Delise *et al.*[7] described a 70% of freedom from AF episodes after slow-pathway ablation in patients with evidence of both AVNRT and AF. Interestingly, this study showed that the AF recurrences after slow-pathway ablation were much more common in patients with structural heart disease than in patients without.[7] The incidence of inducible supraventricular tachycardias in patients referred for AF ablation has been investigated as well.[8,9] Katritsis *et al.*[8] showed that arrhythmias other than AF were inducible in 31 (7.6%) of their AF ablation patients. In this study, an ablation strategy addressed only at the SVT elimination was performed in 13 patients (71% represented by AVNRT), while in the other subjects a combination of tachycardia and AF ablation procedure or only AF ablation was performed.[8] Atrial fibrillation recurrences during the follow-up occurred in 40% of patients that underwent a combined AF-SVT ablation or AF-only ablation, and in 23% of subjects with only SVT ablation.[8] Sauer *et al.*[9] observed AVNRT inducibility during EPS in 27 of 629 patients referred for AF ablation. Only 13 of these patients underwent AVNRT ablation without PV isolation.[9] Twelve of these remained free from AF recurrences without any need for antiarrhythmic drug therapy at a mean follow-up of 21 $\pm$ 9 months.[9] Also atrial tachycardia have been identified as a potential AF trigger,[12–14] but conclusive data about the efficacy of this triggering arrhythmia ablation on AF recurrences have not been deeply investigated.

Electrophysiological mechanisms of AF in patients with a triggering SVT have been studied, particularly in patients with WPW.[41,42] Whereas the accessory pathway seems to play a crucial role for the development of AF,[41] other electrophysiological abnormalities, not related to the accessory pathways, have been observed.[42] Those abnormalities include altered atrial refractoriness, increased induction of repetitive atrial firing and increased atrial conduction delay.[42] Such alterations may explain the incidence of AF recurrences in some patients successfully ablated for accessory pathway.[42]

Comments to our results

In our study we observed that 10.1% of subjects referred to our centre for transcatheter ablation of AF were inducible for SVT, such as FAT, AVNRT, and AVRT due to concealed accessory pathways at the EPS. In all those patients, the synchronized tachycardia was previously unknown and only relapses of AF had been documented. In such a population, the EPS revealed to be crucial in order to detect an underlying regular SVT and to define a tailored ablation strategy. We decided not to include in our analysis patients with atrial flutter, taking into consideration that atrial flutter and AF are arrhythmias in complex and particular relationships,[43–45] and it is sometimes difficult to establish a triggering relationship between atrial flutter and AF.

A spontaneous conversion from SVT into AF was seen in 42.3% of patients with both arrhythmias. In the remaining 57.7% we could not directly demonstrate the role of the SVT as an AF trigger. However, the favourable follow-up of these patients, without recurrences of SVTs and with a very low rate of AF relapses seems to further confirm the role of the regular tachycardia as an AF trigger in our patients.

Our ablative strategy targeted only at the elimination of SVT, without pulmonary veins isolation and/or encircling of pulmonary veins ostia, resulted in simpler procedures, without any complication for the patients. This ablative approach was correlated with a very favourable follow-up as well, without evidence of SVT recurrences and with a low rate of relapses of AF (7.7% after a mean follow-up of 21 $\pm$ 11 months), despite the interruption of any antiarrhythmic drug. When compared with the general AF ablation population in our centre, patients with an underlying regular tachycardia appear to be younger and with less structural heart disease. This observation can also explain the very favourable follow-up of this population.

Another aspect to be considered is that two patients (7.7%) of the SVT group affected by hypertension, continued to assume ACE inhibitors and angiotensin receptor blockers after the ablation procedure, while one patient with hypercholesterolemia continued the statin treatment. It is well known that those drugs may have a role in the prevention of AF recurrences.[46–48] However, we must consider that those three patients are a minority in our study group. Moreover, those patients continued to assume the same drugs that they were taking before the ablation procedure (*Table 1*).

In our opinion, based on our data and on the available data in the literature,[5–11] every patient with an indication for AF ablation should perform an EPS in order to exclude the inducibility of an underlying SVT. This is particularly true for patients with paroxysmal AF and without evidence of significant structural heart disease. We believe that there is enough evidence to sustain that subjects with the presence of both SVT and AF should be addressed to a simpler and safer ablative procedure, targeted only at the SVT suppression.

Conclusions

A small but very important proportion of subjects candidates for AF ablation may have an underlying SVT that can act as a trigger of AF. Those subjects tend to be younger and with less structural heart disease when compared with the general AF ablation population. The identification of such patients can be possible by means of a careful arrhythmic history reconstruction and/or by means of an EP study. Those patients may benefit of a simpler ablative approach targeted only at the underlying arrhythmia elimination without any other extra lesion.

Conflict of interest: none declared.

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