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Athens, Greece 26 June 2013. Two important studies were released at the Late Breaking Clinical Trials session II at EHRA EUROPACE 2013. The PREFER AF study found that Oral anticoagulation is now used in over 85% of patients with atrial fibrillation (AF) eligible for therapy. And ISSUE (the International Study on Syncope of Uncertain Aetiology) determined that cardiac pacing is more effective in patients with presumed neurally mediated syncope (NMS) and asystolic episodes in which tilt table testing proves negative (TT-), than in patients in which the tilt table testing proves positive (TT+).

**PREFER AF**

The PREFER AF registry study, which provides a 'snapshot' of clinical practice across five European countries taken in 2012, revealed that novel oral anticoagulants are now used by 6.1% of AF patients, and that use of rhythm control mediations and catheter ablations have also increased.

"PREFER AF illustrates changes in management of patients with AF since the last ESC guidelines. The registry shows that oral anticoagulant therapy is now much more widely used than in the German Competence Network on Atrial Fibrillation (AFNET) and the Euro Heart Survey registries on AF and suggests that European clinicians are using guidelines well. The rapid uptake of new oral anticoagulants suggests that these drugs are filling a therapeutic gap," said Professor Paulus..."
Kirchhof, presenter of the study from the University of Birmingham, UK. The investigators believe the study represents the largest European registry on AF to date.

The ESC Guidelines for the Management of atrial fibrillation, published in 2010, incorporated several 'evolutionary' changes in the management of AF including the concept of active AF screening to initiate therapy before complications had occurred and furthermore emphasized that continuous oral anticoagulation was indicated for the majority of AF patients since almost all are at increased risk of stroke.

Between January 2012 and January 2013 the PREvention of thromboembolic events –European Registry in Atrial Fibrillation (PREFER) registry enrolled consecutive patients with AF from 461 centres in France, Germany, Italy, Spain and UK. Altogether 42% of patients were office based, 53% hospital based and 89% were treated by cardiologists. "Since practice patterns can be influenced by the type of physicians, we felt it was important to recruit patients from a number of different settings," explained Prof. Kirchhof.

Results showed that of the 7,243 evaluable patients enrolled, 30% had paroxysmal AF, 24% persistent AF, 7.2% long standing persistent, and 38.8% had permanent AF.

When medications were examined it was found that 66.3% of patients (4799) received a vitamin K antagonist (VKA) as monotherapy; 9.9% of patients (720) received VKA and an antiplatelet agents in combination; and 6.1% received novel oral anticoagulants (dabigatran, rivaroxaban or apixaban). Furthermore, antiplatelet agents alone were given to 11.2% of patients (808) and 6.5% of patients (474) received no antithrombotic therapy at all.

Altogether 78.6% of patients were adequately rate controlled, using a
mean heart rate of 60 to 100 bpm as the definition.

Rhythm control therapy was given to 66.7% of patients, with rhythm control consisting of electrical cardioversion in 18.1% of patients; pharmacological conversion in 19.5%; amiodarone in 24.1%; flecainide in 10.5%; sotalol in 5.5%; dronedarone in 4% and other antiarrhythmic drugs in 3.1% and catheter ablation in 5%. However, over 80% of patients still suffered from AF symptoms despite good rate control.

"We were surprised and puzzled by the high number of patients who suffer from AF despite good rate control," said Prof. Kirchhof. "This indicates that we have more work to do to develop tools to better prevent AF and possibly to better maintain sinus rhythm in the future."

The ongoing EAST (Early treatment of atrial fibrillation for stroke prevention trial) study 4 is currently testing whether early use of rhythm control therapy can prevent adverse cardiovascular outcomes in patients with AF compared to usual care.

**ISSUE (international study on syncope of uncertain aetiology)**

The second important study at the session, the ISSUE 3 registry, showed that diagnosis of NMS, using ESC guidelines on Diagnosis and Management of Syncope, could be confirmed with an implantable loop recorders (ILR) in 87% of patients.

"By showing that NMS tilt-negative asystolic patients benefit most from cardiac pacing, the study inverts previous knowledge on indications for pacing. Prior to this registry, cardiac pacing for NMS had only been evaluated in patients with positive tilt test responses and no indications had existed for patients with negative tilt test results," said Professor Michele Brignole, presenter of the study.
ISSUE was a prospective registry set up to analyse the diagnostic yield of ILRs in specific subgroups of patients with syncope of uncertain aetiology. The registry took place in Italy, Spain, Germany, France, Canada, The Netherlands and UK. For the ISSUE 3 registry, between July 2006 and November 2010, 504 patients with suspected NMS, according to criteria laid down in guidelines, had an implantable loop recorder (IRL) fitted. Entry criteria included being older than 40 years and having experienced more than three episodes of syncope in the previous two years thought to be neurally mediated. Guidelines6 state that a likely diagnosis of NMS can be made when patients have a consistent history and competing diagnoses have been excluded.

Results show that a confirmed diagnosis could be achieved in 187 patients, with ILR findings in 162 of these patients (87%) being consistent with a likely diagnosis of NMS, and IRL findings in 25 patients (13%) allowing NMS to be ruled out. Of the 162 patients with IRL findings suggesting NMS 99 were found to be asystolic (where the heart stops beating for a short period of time) and 63 hypotensive (where blood pressure falls).

Altogether 52 patients received a pacemaker, of which 26 had a positive table tilt test result (TT+) and 26 patients a negative table tilt test (TT-) result. After 21 months the syncope recurrence rates were 55% (95% CI 29-85) in TT+ patients fitted with the pacemaker versus 5% (95% CI 1-32) in TT- patients fitted with the pace maker (p=0.004). When the recurrence rate of 55% in the TT+ patients was compared to 44 untreated patients (who acted as controls) who had recurrence rates of 64% the difference was not found to be statistically significant (p=0.75).

For patients with negative table tilt tests, the observed 5% recurrence rate was similar to that observed for patients paced for cardiac intrinsic bradycardia. "Thus, pacemaker therapy can be offered to these patients
with the same confidence as it can in patients with sick sinus syndrome or AV block," said Prof. Brignole. "Such patients can be reassured that, after pacemaker implantation, they'll likely be free from reoccurrences of syncope."

But before pace maker therapy is offered to patients with TT+ even if they have experienced an asystolic response during the tilt test patience should be cautioned they may have reoccurrences. "Although some benefits may still be possible in terms of reduced syncope burden, patients should be informed that they'll likely have some recurrences despite pacing," said Prof. Brignole.

Most of the misdiagnoses in the study were due to intrinsic cardiac arrhythmias which were largely unpredictable from baseline characteristics. "This aspect, which has not yet been clarified in the literature, may be relevant in clinical practice," he said, adding that it further justifies the usage of the ILR diagnostic tool.

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