CABANA trial: disappointing results?

Preliminary results of the CABANA study\textsuperscript{1,2} would seem not to document statistically significant differences in the comparison of transcatheter ablation vs. antiarrhythmic drugs (AAD) with regard to the composite of death, disabling stroke, severe bleeding, and cardiac arrest over a median 5-year follow-up among patients with history of atrial fibrillation (AF). However, in CABANA trial, transcatheter ablation has significantly reduced AF recurrences, compared with chronic AAD therapy.\textsuperscript{1} Therefore, the lower burden of AF relapses using transcatheter ablation has not resulted in a significant improvement of the primary endpoint.\textsuperscript{3} Moreover, at least judging from the preliminary results of the CABANA trial\textsuperscript{1} the study purpose does not seem to be a comparison of rate control strategy with ablation. Indeed in the arm assigned to pharmacological therapy, ‘drug therapy could be either for rate or rhythm control’.\textsuperscript{3} More exactly, ‘rhythm control with 1–4 drugs was attempted in 87% of patients, in addition to rate control’, according to Markides.\textsuperscript{4} Indeed, I have observed that there is an intertwining of information. Part of this information arises from the communication of Dr Poole—presented at the Congress of the American College of Cardiology 2018 and subsequently at the ESC 2018 Congress, and reported attached to the present letter—, which makes a rather succinct description of the study and only provides some preliminary results. Further information instead originates from comments and explanatory statements by electrophysiologists and/or clinical cardiologists who actively participated in the study\textsuperscript{3–5} which involved as many as 110 centres in 10 countries.\textsuperscript{1}

My first impression is that there are two currents of thought, the first that grants credit exclusively to the results of the analysis conducted according to the principle of intention to treat,\textsuperscript{1} the second instead that attributes great relevance to inferences and results derived from the ‘on treatment’ analysis.\textsuperscript{4}

Indeed CABANA trial in the intention to treat analysis, has failed to support the hypothesis that catheter ablation for the purpose of suppressing AF is superior to AAD therapy in improving the primary composite endpoint and mortality. However, it is worthy to mention that about 30% of patients originally assigned to AAD arm decided to undergo transcatheter ablation for the relief of symptoms after several months or years of pharmacological therapy. According to the advocates of the ‘as treated’ approach,\textsuperscript{5} cross-over rates in both directions and the lower than expected event rate in the drug arm might have substantially prejudiced the validity of the study as well as the reliability of conclusive inference that no significant differences exist between catheter ablation and AAD therapy with regard to primary composite endpoint. In fact according to the ‘as treated’ analyses, ablation would have demonstrated superior efficacy compared to AAD therapy regarding mortality.

However, my personal opinion does not diverge from the recommendations of pharmacoepidemiologists who assign primary relevance to principle of intention to treat. My personal view includes rather another concept, that is AF, especially when treated with judicious anti-coagulation coupled with appropriate pharmacologic modulation of AV node conduction, is not associated with an increased risk of death compared to ablated patients. Therefore, even though the CABANA trial demonstrates that protection against the AF relapses is better using ablation (time to first AF recurrence for ablation vs. AAD therapy: hazard ratio 0.53, 95% CI 0.46–0.61; \(P<0.0001\)), this does not translate into a significant improvement of prognosis in the mid–long term. Thus, based on the results of the CABANA trial, it is reasonable to state that ablation ameliorates the quality of life by reducing the burden of paroxysmal or persistent AF episodes, but its impact on the long-term clinical endpoints does not differ from that exerted by the pharmacologic approach.

A debate about these findings would then be more than ever appropriate and useful.

Conflict of interest: none declared.

References

1. Poole JE. Catheter Ablation vs ANtiarrhythmic Drug Therapy for Atrial Fibrillation—CABANA. Communication presented at the ESC Congress, Munich, Germany, 26 August 2018 (abstract) https://www.acc.org/latest-in-cardiology/clinicaltrials/2018/05/10/15/57/cabana (enclosed with the present manuscript as supplementary material). (15 September 2018).

Renato De Vecchis*
Preventive Cardiology and Rehabilitation Unit, DSB 29 “S. Gennaro dei Poveri Hospital”, via S.Gennaro dei Poveri 25, Napoli 80136, Italy

*Corresponding author. Tel: +393483313530, Fax: +39 0812543145, Email: deveccis.erre@virgilio.it