# USA and Europe different in aldosterone antagonists use in heart failure

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A study published today, in *JAMA* (October 21) by Nancy M. Albert and colleagues, exploring aldosterone antagonist usage among US patients hospitalised with heart failure, found that only one-third of patients meeting current US Clinical Practice Guidelines criteria were actually being treated (1).

Furthermore, the observational analysis of 43,625 patients admitted with heart failure and discharged home from 241 hospitals participating in the 'Get With IT Guidelines', showed that prescription of aldosterone antagonists at discharge varied widely among clinicians. Additionally the study revealed aldosterone antagonist use is less common among patients who are elderly, white, have a lower systolic blood pressure, who do not have an implantable cardioverter-defibrillators or pacemakers, who do not have a history of alcohol use or depression, and have a history of renal insufficiency. Finally, the study showed that in contrast to prior reports, rates of inappropriate use were infrequent - only 0.5% of patients received therapy with documented contraindications, and 2.7% received therapy with higher than recommended creatinine levels.

Commenting on the study for the European Society of Cardiology (ESC), Professor Kenneth Dickstein from the University of Bergen, Stavanger University Hospital, Norway, said: "This is an interesting paper that provides an overview of real life practice in the US. It was really encouraging to see that contrary to previous reports, inappropriate use of aldosterone antagonists is now really rare."

Professor Dickstein added that it is worth noting that the *JAMA* paper included patients with a first episode of heart failure or with significant heart failure symptoms developing during hospitalisation.

"This not strictly the population covered in the Guidelines. Therefore the lower rates of aldosterone antagonist use found in the study cannot be considered unexpected," he said.

The study, said Prof Dickstein, who is also Chairman of the Task Force for the ESC's 2008 Clinical Practice Guidelines on Heart Failure, reveals fundamental differences in approach to both the writing of guidelines and treatment of heart failure between the US and Europe. "In Europe our guidelines are somewhat more conservative. But in contrast our actual use of therapy is more liberal," he said.

ESC Guidelines for aldosterone antagonist use in heart failure, Prof Dickstein explained, are based around a single study - the RALES trial, where patients with severe heart failure were randomised to spironolactone or placebo (2). A notable difference between the American and European guidelines is that the AHA/ACC guidelines also extrapolate from the post infarction EPHESUS (3) trial of an aldosterone antagonist, which also had a positive outcome, but was not strictly conducted in a heart failure population.

The AHA/ACC Guidelines state that aldosterone antagonists should be recommended in selected patients with moderately severe to severe symptoms of heart failure (NYHA III/IV) and reduced LVEF who are being carefully monitored for renal function and serum potassium (3). The ESC Guidelines say that low doses of an aldosterone antagonist (unless contraindicated) should be considered for patients with LVEF less than 35 % and severe symptoms of heart failure (ie NYHA III B or IV.) (4)

"While in practice there may seem to be little difference between the Guidelines, European guidelines are somewhat more restrictive in that they consider the level of evidence for aldosterone antagonists to be based on a single trial. Use is only recommended in patients who have been in functional class IV in the last six months,"explained Prof Dickstein.

The Europeans, he added were more conservative in their Guideline writing, adhering to the famous Einstein quote: "In theory, theory and practice are the same. But in practice they are not." "That is why we need randomised clinical trials," said Dickstein.

In real life practice, use of aldosterone antagonists is less restrictive in Europe than the US, he added. "US clinicians are more concerned about off-label use, and therefore more conservative about what they choose to prescribe. European clinicians have greater leeway and more often push the envelope to explore new indications in their clinical practice."

Indeed the current *JAMA* study found that only 32.5 % of patients meeting current US Guideline criteria for aldosterone antagonist therapy were treated, whereas the Euro Heart Failure survey (II) (6) in 2004/2005 showed that the rate of aldosterone antagonist use on hospital discharge was 48 %.

The European Guidelines include an evidence chapter that emphasises that one of the gaps in the current evidence is that it has yet to be shown in a clinical trial whether an aldosterone antagonist reduces morbidity and mortality in patients with mild symptoms of heart failure (NYHA class II).

It is hoped, said Dickstein, that current ongoing studies will add further evidence which will allow Guidelines to extend the use of aldosterone antagonists to patients with milder heart failure. The ongoing studies, are

TOPCAT comparing spironolactone (45mg) versus placebo in 4500 patients with mild HF (NYHA II, EF> 45%) and preserved LV function; and EMPHASIS HF, looking at use of the aldosterone antagonist eplerenone in patients with mild heart failure (NYHA II, Ejection Fraction