Cardiovascular highlights from non-cardiology journals

Lindsay Alistair

*Heart* 2010 96: 1078-1079
doi: 10.1136/hrt.2010.201897

Updated information and services can be found at:
http://heart.bmj.com/content/96/13/1078.full.html

**Email alerting service**

These include:

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To order reprints of this article go to:
http://heart.bmj.com/cgi/reprintform

To subscribe to *Heart* go to:
http://heart.bmj.com/subscriptions
Cardiovascular highlights from non-cardiology journals

**GENERAL CARDIOLOGY**

Novel blood pressure agent shows promise

Natriuretic peptides have a number of beneficial vascular effects: vasodilator and natriuretic properties, reduced sympathetic drive, anti-proliferative effects, and inhibition of the renin–angiotensin–aldosterone (RAAS) system. Inhibition of nephrilysin (neutral endopeptidase 24.11) leads to an increase in natriuretic peptide levels, but on its own this mechanism does not lead to a clinically significant decrease in blood pressure. However, concomitant administration of an inhibitor of the RAAS system could potentially eliminate this problem, thus a novel dual-acting nephrilysin and RASS inhibitor labelled LCZ696 was investigated in this study.

One-thousand, two-hundred and fifteen patients completed 8 weeks of treatment with LCZ696. All patients had mild-to-moderate hypertension and were randomly assigned to LCZ696 at various doses, valsartan, a nephrilysin inhibitor on its own or placebo. Compared to treatment with valsartan alone, patients taking LCZ696 showed significantly greater reductions in mean sitting diastolic blood pressure (mean reduction 2.17 mmHg, p<0.0001, figure 1), sitting and ambulatory pulse pressure, and 24-h ambulatory systolic blood pressure. LCZ696 was well tolerated, and no cases of angio-oedema were reported with the drug — this had been a problem with a previous nephrilysin inhibitor compound, omapatrilat.

**Conclusions**

LCZ696, a novel antihypertensive that inhibits both nephrilysin and angiotensin receptors, provided complementary and additive blood pressure reduction when compared to the use of valsartan alone. Larger scale trials are now needed, but this novel therapeutic approach could potentially confer combined cardiac, vascular and renal protection.


**INTERVENTIONAL CARDIOLOGY**

Optimal duration of dual antiplatelet therapy remains unclear

Dual antiplatelet therapy with aspirin and clopidogrel has become the cornerstone of the treatment of acute coronary syndromes. Although 12 months has become the standard treatment time for most patients, it remains unclear whether longer durations of treatment may provide additional benefit, and in particular whether this would allay fears regarding the risk of late stent thrombosis associated with the use of drug-eluting stents (DES).

To address some of these questions, the authors present results from two studies, REAL-LATE (Correlation of Clopidogrel Therapy Discontinuation in Real-World Patients Treated with Drug-Eluting Stent Implantation and Late Coronary Arterial Thrombotic Events) and ZEST-LATE (Evaluation of the Long-Term Safety after Zotarolimus-Eluting Stent, Sirolimus-Eluting Stent, or Paclitaxel-Eluting Stent Implantation for Coronary Lesions — Late Coronary Arterial Thrombotic Events), which were merged due to slow recruitment and similar design. In both these studies, patients had undergone implantation of a DES and successfully completed 12 months of dual antiplatelet therapy without adverse effects. Patients were subsequently randomised to either continuation of dual therapy or aspirin alone in an open label fashion. The primary end point was a composite of myocardial infarction or death from cardiac causes. Between July 2007 and September 2008, 2701 patients were enrolled at 22 centres in South Korea with 1387 assigned to clopidogrel plus aspirin and 1344 to aspirin alone. Nearly half of these patients had multivessel disease, and more than 60% had an acute coronary syndrome as the indication for their percutaneous coronary intervention (PCI) (although less than half met criteria for ST elevation myocardial infarction (STEMI) or non-ST elevation myocardial infarction (NSTEMI)). The median duration of follow-up was 19.2 months. The risk of the primary outcome at 2 years was 1.8% with dual antiplatelet therapy, as compared with 1.2% with aspirin monotherapy (HR 1.65, 95% CI 0.80 to 3.36, p=0.17). Additionally, the individual risks of myocardial infarction, stroke, stent thrombosis, need for repeat revascularisation, major bleeding and death from any cause did not differ significantly between the two groups.

Therefore, the results from the study suggest that a prolongation of dual antiplatelet therapy is not beneficial and in fact there are some hints that it may be detrimental with a statistically non-significant increase in the composite of myocardial infarction, stroke or death from any cause (HR 1.73, 95% CI 0.99 to 3.00, p=0.051) and in the composite of myocardial infarction, stroke or death from cardiac causes (HR 1.84, 95% CI 0.99 to 3.45, p=0.06). These results in particular are counterintuitive and are very much at odds with data from most previous studies, and as such bring into play the role of chance in these findings. Unfortunately, it is difficult to glean a great deal from this study to guide clinical practice as it is an interim analysis of two ongoing, underpowered studies, which, even when combined, have an event rate less than the 25% that was anticipated — raising questions of the risk profile of the enrolled patients.

**Figure 1** Mean sitting systolic (top) and diastolic blood pressure changes.
Conclusions
In this analysis of two combined trials, no clear benefit was seen from continuing dual antiplatelet therapy for more than 12 months. Further trials on this issue are under way.


Molecular Cardiology
Coronary arteries form from reprogramming of venous cells
The cellular and developmental origins of the coronary arteries remain relatively poorly studied; determining how coronary vessels arise during development, are maintained in adult life and remodel under pathological conditions could further our understanding of diseases such as atherosclerosis.

Red-Horse et al carried out anatomical and histological analysis of coronary vessel development during mouse embryogenesis by using endothelial markers. Coronary vessel progenitors were found to arise from angiogenic sprouts of the sinus venosus, which then differentiate: invading cells differentiate into arteries and capillaries, whereas cells that remain on the surface differentiate into veins. Position-specific cardiac signals trigger the differentiation into arteries, capillaries or veins.

Conclusions
This study redefines the conventional view that coronary vessels form from proepicardial cells that undergo an epithelial-to-mesenchymal transition. Understanding the process of coronary arterial development could lead to alternative revascularisation strategies in future.


Journals scanned

Reviewers
Dr Alistair C Lindsay, Dr Hussain Contractor, Dr Jonathan Spiro

Competing interests None.

Provenance and peer review Not commissioned; not externally peer reviewed.