Impact of asynchronous ventricular activation on pro-inflammatory cytokines and oxidative stress in paced patients

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METHODS
We enrolled consecutive patients with sick sinus syndrome, first degree atrioventricular block (PR interval > 200 ms), and normal intraventricular conduction, who required a dual chamber pacemaker implantation.

The pacemaker was initially programmed as AAIR with a basic rate of 40 bpm for a three month period and then the patients were randomised for 15 days to either AAIR or DDDR pacing, with a basic rate of 60 bpm, and the study continued in a crossover design. During DDDR pacing, the atrioventricular activation was fully paced and the atrioventricular interval was the one that ensured the best diastolic filling. At the end of each 15 day randomisation, but not at baseline, blood samples were taken to evaluate LP, IL-6, and TNFα in patients with sick sinus syndrome and a permanent dual chamber pacemaker during physiological and RAVP, as produced by AAIR and DDDR permanent pacing, respectively.

RESULTS
A total of 25 patients (15 male; mean age 56 (8) years) were included. Ejection fraction, left atrial dimension, and wall motion indices were normal throughout the study and showed no significant changes. Anterior systolic intraventricular septal motion was observed in 22 patients during physiological and RAVP.

In contrast to the acute study, LP and IL-6 concentrations were significantly lower during the one hour AAIR and DDDR pacing period compared to those at the end of the AAIR pacing period (LP 388.7 (110.2) μmol/l, IL-6 3.2 (0.9) pg/ml, and TNFα 102.6 (3.1) pg/ml in AAIR vs 351.2 (102.6) μmol/l, 3.1 (0.9) pg/ml, 2.7 (0.8) pg/ml in DDDR, p = 0.73, p = 0.21, p = 0.58, respectively).

DISCUSSION
Our study demonstrates for the first time that AVA caused by RAVP in patients with sick sinus syndrome leads to an undesirable increase in pro-inflammatory cytokines and LP.

Abbreviations: AVA, asynchronous ventricular activation; IL-6, interleukin-6; LP, lipid peroxides; RAVP, right apical ventricular pacing; TNFα, tumour necrosis factor α
Published studies demonstrate that preserving the normal ventricular activation sequence acutely improves the cardiac systolic and diastolic performances and myocardial blood flow. On the other hand, it has been postulated that pro-inflammatory cytokines and oxidative stress are increased during ventricular dysfunction. Thus, the haemodynamically advantageous AAIR pacing may prevent the deleterious production of increased IL-6 and LP. Our results could have even more serious implications for patients with myocardial ischaemia or heart failure. The non-significant increase of TNFα may be because of the short study period and DDDR permanent pacing in the long term might lead to an increase of TNFα plasma concentrations in a similar manner.

We had no data concerning the baseline values for plasma concentrations of cytokines and LP. However, our aim was only to compare these two modes of pacing. In any case, no certain conclusions could have been drawn, since our data could have been influenced by differences in heart rate before and after the initiation of pacing.

Irrespective of the relation between cytokines, LP, and the pathophysiology of left ventricular dysfunction during AVA, our findings support the existing data from the literature and underline the importance of programming a permanent pacemaker in such a way as to ensure the most physiological ventricular excitation sequence possible.

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