

Abstracts

Junior Members Forum, Thursday 23 November 2006

Ulster Medical Society Rooms,
Whitla Medical Building, Belfast

PROGRAMME

- 8.00pm Introduction – Prof Dennis Johnston, UMS Junior Vice President
- 8.10pm Dr Ben Glover. Low tilt biphasic waveform studies
- 8.30pm Dr Gareth Lewis. Kidney slit diaphragm genes in type 1 diabetes.
- 8.50pm Dr Chris Lockhart. Waveform Analysis in Diabetes
- 9.10pm Discussion
- 9.30pm Tea and Close

The use of a low tilt biphasic waveform lowers the defibrillation threshold for the internal cardioversion of atrial fibrillation

BM Glover^{1,2}, CJ McCann^{1,2}, MJ Moore^{1,2}, SJ Walsh^{1,2}, G Manoharan¹, MJ Roberts¹, JD Allen², AAJ Adgey¹.

Regional Medical Cardiology Centre¹, Royal Victoria Hospital, Belfast, Queens University², Belfast.

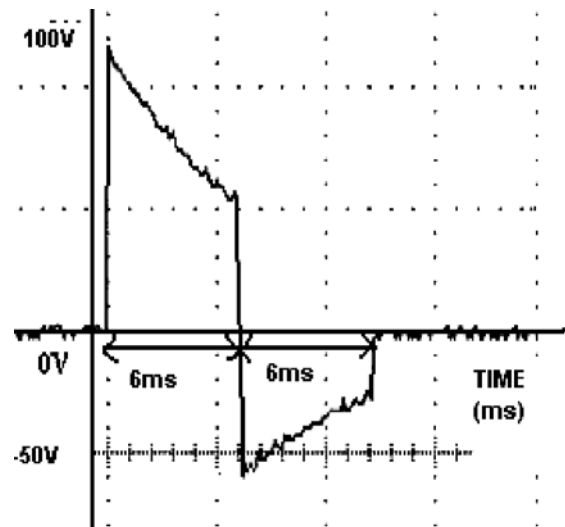
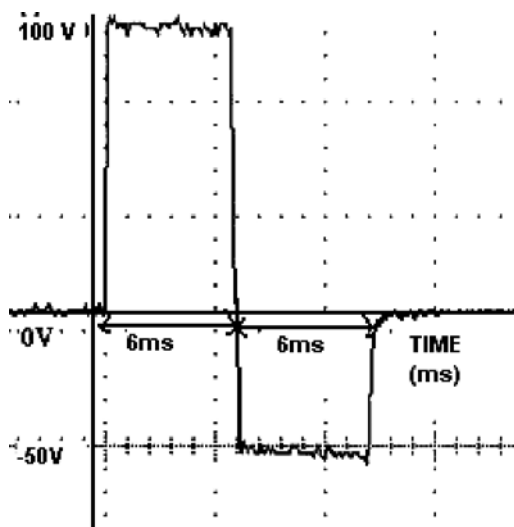
Purpose: Conventional defibrillators used for the internal cardioversion of atrial fibrillation (AF) employ high tilt

waveforms generated by a capacitor based discharge. We have developed a biphasic waveform with low tilt. This was compared with a conventional waveform of equivalent duration (6/6ms) and voltage.

Methods: Patients were randomised to receive either the low tilt waveform or a conventional waveform. Defibrillation electrodes were positioned in the right atrial appendage and distal coronary sinus. Peak voltage was increased in a stepwise progression from 50V to 300V. Shock success was defined as return of sinus rhythm for ≥ 30 seconds.

Results: The low tilt waveform resulted in successful termination of persistent AF in 10 of 13 cases (77%) at a mean voltage of 223V versus the conventional waveform in 2 of 12 cases (17%) at a mean voltage of 270V ($p = 0.002$). In patients with induced AF the mean voltage for the low tilt waveform was 90V and for the conventional waveform was 158V ($p=0.005$).

Conclusions: The low tilt biphasic waveform was more successful for the internal cardioversion of both persistent and induced AF. This waveform could be useful for the termination of both persistent and induced AF during ablation procedures in order to restore sinus rhythm at a low voltage.



The novel low tilt biphasic waveform (left) versus a conventional tilted biphasic waveform (right)

Association of common gene polymorphisms in kidney slit diaphragm genes with nephropathy in type 1 diabetes.

G Lewis¹, DA Savage¹, CC Patterson², AP Maxwell¹.

¹Nephrology Research Group, Queen's University Belfast, Belfast, Northern Ireland. ²Department of Epidemiology and Public Health, Queen's University Belfast, Belfast, Northern Ireland.

Objective: Integrity of the kidney slit diaphragm (SD) is essential for proper glomerular filtration. DNA sequence mutations in genes encoding the protein components of the SD can cause severe proteinuria. It is hypothesised that common DNA polymorphisms within SD genes may predispose to the development of proteinuric renal disease such as diabetic nephropathy (DN).

Methods: The genes NPHS2, CD2AP, NPHS1, Kirrel2, ACTN4, NEPH1 and TJP1 were screened by denaturing high-performance liquid chromatography for DNA polymorphisms in 15 DN cases and 15 type 1 diabetic controls without nephropathy. All coding and regulatory regions were examined and the population frequency of the detected variants characterised in 48 healthy controls. Haplotype-tagging single nucleotide polymorphisms (htSNPs) were deduced for each gene utilising the variants occurring at 5% frequency.

Results: A total of 128 polymorphisms were detected. Thirty htSNPs and six potentially functional variants were genotyped in a case-control association study (cases=223, controls=366). All patients were Caucasians with type 1 diabetes diagnosed before 31 years. Cases had persistent proteinuria +/- renal failure, developing after at least 10 years duration of diabetes. Controls had a minimum duration of diabetes of 15 years, were not receiving any anti-hypertensive therapy and had no evidence of microalbuminuria on repeated testing. Allele and genotype frequencies for all polymorphisms, in addition to the haplotype distributions in each gene, were compared between cases and controls. Three variants and haplotypes in NPHS1, Kirrel2 and ACTN4, all located within a 3 Mb region on 19q13, were associated with DN ($P < 0.05$).

Conclusions: Common variation in the SD genes studied may account for a component of the inherited predisposition to DN. Replication of these results in a separate population is necessary to confirm whether or not a susceptibility region for DN exists on 19q13.

Waveform Analysis in Diabetes - A marker for Cardiovascular Risk Stratification

CJ Lockhart¹; PK Hamilton¹, C Quinn¹, C Agnew², RC McGivern², GE McVeigh¹.

¹Department of Therapeutics and Pharmacology. School of Medicine. Queens University Belfast.

²Medical Physics Agency, Royal Victoria Hospital, Belfast.

Objectives of Research: Characteristic changes in the arterial

pressure pulse contour accompany risk factors for and disease states associated with an increase in cardiovascular events. Such changes in waveform morphology, recorded by invasive and non-invasive techniques in large arteries, indirectly implicate altered structure and function in microvascular beds as the primary sites for vascular adaptations associated with ageing and disease. Dysfunction of the vascular endothelium is a hallmark of most conditions that are associated with atherosclerosis, and plays a pivotal role in the pathogenesis of atherosclerosis and its complications.

The over-arching aims of this study are:

1. To determine if quantitative analysis of velocity flow waveforms, recorded from the brachial artery, can identify and track local changes in vascular tone in response to nitric oxide modulation. We postulate that altered brachial flow waveform morphology in response to NO modulation, is apparent before a change in the arterial diameter can be detected. Furthermore, a sensitive non-invasive marker capable of detecting changes in NO bioavailability, and thus endothelial function, could have major therapeutic importance in the clinical setting.

2. To show that quantitative analysis of Doppler flow velocity waveforms, recorded in the ocular circulation, can sensitively detect and track local changes in micro vascular haemodynamics of type I diabetics; and in particular, to relate such waveforms to changes in geometry and tone of the microvasculature i.e. mapping of the retinal arteriolar circulation, in response to inhaled oxygen and carbon dioxide.

Methods: Characterisation of Doppler flow velocity waveforms by identification of the systolic and diastolic excursions of flow (or pulsatility) during the cardiac cycle have been employed to estimate vascular resistance of the microvascular networks, downstream to the measurement site. In our department we have shown that time-domain and frequency-domain analysis of Doppler flow waveform morphology recorded in the ophthalmic and central retinal artery clearly discriminates between patients with type 2 diabetes mellitus and age-and-sex matched control subjects. Analysis of waveforms recorded from the carotid artery in these patients did not discriminate between the 2 groups. Waveform analysis also sensitively detected and tracked the haemodynamic effects of the administration of donors and inhibitors of nitric oxide in the ocular microcirculation. The development of more advanced waveform analysis techniques is currently underway.

Conclusions and future work: These preliminary data suggest the ability to directly evaluate and monitor the status of specific microcirculatory beds of interest rather than inferring general changes in the microcirculation from pulse waveforms recorded from large muscular and elastic conduit arteries, identifies structural and functional abnormalities in specific target organs. If endothelial dysfunction (ED) is indeed the substrate for the development and progression of arteriosclerosis, the ability to detect ED and to monitor sub clinical vascular disease holds potential to further refine cardiovascular risk stratification and preventive therapy.