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The Second Vasovagal Pacemaker Study (VPSII)

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The Second Vasovagal Pacemaker Study (VPSII): A double-blind randomized controlled trial of pacemaker therapy for the prevention of syncope in patients with recurrent severe vasovagal syncope. Three previous small randomized trials have reported that pacemaker therapy is very beneficial for patients with severe recurrent vasovagal syncope. However these trials were not double blind and were thus at risk of bias in assessment of outcomes and of a 'placebo-effect' of surgery. To determine if pacing therapy reduces the risk of syncope in patients with vasovagal syncope. A double-blind randomized trial of pacemaker therapy was performed. After implantation of a dual chamber pacemaker, 100 patients from 15 centres were randomized, double blind, to receive dual chamber pacing (DDD) with rate drop response or to have only sensing with no pacing (ODO). Patients were followed for up to 6 months and the primary outcome of the study was time to first recurrence of syncope. Results: Patients were well matched as to baseline characteristics. In the year prior to randomization patients had had a median of 4 episodes of syncope. No patients were lost to follow up. Of the patients randomized to ODO, 22 of 52 (42%) had recurrent syncope within 6 months, compared to 16 of 48 (33%) of the patients in the DDD group. The cumulative risk of syncope at 6 months was 40% (95% confidence interval 25%, 52%) for the ODO group and was 31% (95% confidence interval 17%, 43%) for the DDD group. The relative risk reduction in time to syncope with DDD pacing was 30% (95% confidence interval -33%, 63%, $p = 0.14$ one-sided). Lead dislodgement or repositioning occurred in 7 patients, one patient had vein thrombosis and another had pericardial tamponade leading to removal of the pacemaker system. One patient had infection involving the pacemaker generator. Conclusions: This double blind randomized trial does not confirm the results of earlier smaller unblinded randomized trials. Because of the weak evidence of efficacy of pacemaker therapy and the risk of complications, pacemaker therapy should not be recommended as first line therapy for patients with recurrent vasovagal syncope.

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New Trial Data on Prevention: Potassium and CV Risk in Hope

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Introduction: Hypokalaemia may be hazardous. Methods: Potassium was measured in 9,297 patients in HOPE, & was <3.5 in 137. Results: The combined primary outcome (cardiovascular death, myocardial infarction, or stroke) increased with hypokalemia (22.6% vs 15.5%, p 0.023, hazard ratio 1.44). Hyperkalemia conferred no hazard Hypokalemia was more prevalent in women, in hypertensives, & with diuretics. Ramipril benefit was independent of potassium. Less patients on ramipril had hypokalaemia ($p = 0.005$), including those on diuretics (3.8% v 6.5%, $p = 0.07$). Conclusion: In high risk people hypokalemia increased the risk for cardiovascular events, while hyperkalemia did not. Ramipril was not associated with increased risk with hyperkalemia, but mitigated the diuretic induced risk of hypokalaemia; the latter may increase with increased diuretic use after ALLHAT. A diuretic/ACE-Inhibitor combination appeared safe, & may be even more popular after the ANBP-2 trial, which contrary to ALLHAT favoured an ACE-I over a thiazide. HPS & ASCOT favour statins in addition.

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The Role of Multisite Atrial Pacing in Rhythm Control in AF: Insights from Sub-analyses of the Dual Site Atrial Pacing for Prevention of Atrial Fibrillation Study

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Novel pacing modes are being proposed for the prevention or reversion of atrial fibrillation (AF). High right atrial (RA) pacing and septal pacing have not individually reduced arrhythmic events in patients with AF in controlled trials. The DAPPAF trial compared the effectiveness of overdrive high right atrial single and dual site right atrial pacing as compared to demand pacing in prevention of recurrent symptomatic AF in patients with AF & bradyarrhythmias. Methods: From September 1996 to November 2000, 120 patients with documented symptomatic AF were enrolled and followed in a prospective randomized single blind crossover multicenter trial. 73 males & 45 females, mean age 66 $\pm$ 11 yrs with recurrent symptomatic AF (paroxysmal in 82 pts, persistent >72 hrs in 30 pts & persistent >30 days in 6 pts) were enrolled. Baseline AF event frequency was $\geq$1 /day in 40 pts, 1/week in 43 pts, <1/week in 30 pts, & unknown in 5 pts. Patients were implanted with dual site right atrial pacing systems and randomly assigned to six-month treatment periods in overdrive dual, overdrive single or demand pacing. Three primary endpoints (time to first AF recurrence, patient quality of life & tolerance/safety) and several secondary endpoints (device detected sustained AF, atrial & ventricular function indices, & composite endpoints) were examined. Results: Only DAP was significantly effective in preventing recurrent AF and prolonging time to first symptomatic AF recurrence in the presence of class 1 & 3 antiarrhythmic drug therapy; it was more effective than H.A. pacing in reducing asymptomatic AF event frequency; DAY alone prevented left ventricular and left atrial dilatation seen with D'ETRE pacing in this population due to improved left atrial transport; in patients with persistent AF or after Sawtell therapy, DAY maintained efficacy while H.A. pacing showed attrition in effectiveness. DAY was better tolerated than H.A. pacing, with fewer crossovers and comparable safety to H.A. pacing. Conclusions: DAY is an important therapeutic tool in an "hybrid" strategy for management of drug-refractory AF. It offers antiarrhythmic and hemodynamic benefits and can have therapeutic effects on symptomatic and asymptomatic paroxysmal and persistent AF. It can facilitate efficacy of other antiarrhythmic therapies in AF. Further study of its antiarrhythmic effects with hybrid drug and ablation therapies is now in progress, and long-term use in an "hybrid" strategy has been reported in large pilot studies.

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Trial to Evaluate the Management of PSVT During Electrophysiologic Study with Tecadenoson (TEMPEST)

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Introduction: Tecadenoson, a selective A_1 adenosine derivative,prolongs AV nodal conduction without A_2-mediated reductions in BP or A_{2B}/A_3-mediated bronchospasm. The primary study objective was to assess the rate of therapeutic conversion of PSVT without high degree AV block. Methods: This randomized, double-blind, placebo-controlled study enrolled PSVT patients in need of electrophysiologic study. PSVT was induced, sustained for $\geq$2 minutes and first IV bolus of study drug administered. If PSVT persisted after 1 minute, a second bolus was administered. The five tecadenoson regimens were 75μg/150μg (A), 150μg/300μg (B), 300μg/600μg (C), 450μg/900μg (D), 900μg/900μg (E) vs placebo. Results: Therapeutic conversion rate of each tecadenoson regimen was statistically significant versus placebo (ITT; $n = 181$; $p < 0.0005$). Higher regimens converted PSVT after the first dose in most patients ($p < 0.001$). Median time to conversion was $\leq$1 minute. No apparent dose-dependent increase in AE frequency was observed. Conclusion: Each tecadenoson regimen rapidly converted PSVT to sinus rhythm in a dose-dependent manner. In TEMPEST, tecadenoson regimens were identified that rapidly converted 90% of patients without significant adverse symptoms or hemodynamic effects.

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The Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial

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Introduction: The devices used to prove the benefit of ICD therapy had only VVI pacing but most current ICD devices provide dual chamber pacing therapy. The DAVID trial sought to measure the impact of dual chamber pacing at 70 bpm (DDDR-70) vs. ventricular backup pacing at 40 bpm (VVI-40) in patients with standard indications for ICD implantation but without indications for bradycardia pacing. Methods: This single-blind, multicenter, parallel-group, randomized clinical trial enrolled 506 patients with indications for ICD therapy between 10/2000 and 9/2002. All patients had an LVEF $\leq$0.40, no indication for pacemaker therapy and no persistent atrial arrhythmias. ICDs with dual chamber, rate-responsive pacing capability were implanted and programmed to VVI-40 or DDDR-70. Results: The combined endpoint of mortality or hospitalization for congestive heart failure (CHF) at one year was 16.1% (VVI-40) vs. 26.7% (DDDR-70), ($p \sim 0.03$), mortality 6.5% vs. 10.1% ($p \sim 0.15$) and CHF hospitalization 13.3% vs. 22.5% ($p \sim 0.07$). Conclusion: For ICD patients, DDDR-70 pacing exhibits no clinical advantage over VVI-40 pacing and may increase CHF and mortality.

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Revelation® Tx Microcatheter Maze Procedure Successfully Treats Paroxysmal AF

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Introduction: Currently the recommended treatment for atrial fibrillation is pharmacologic therapy. The ability of antiarrhythmic drugs to maintain normal sinus rhythm ranges from 39% to 79% in the first year. A multicenter, prospective clinical study involving 20 centers and 80 subjects has shown promising results for an effective, minimally invasive treatment of paroxysmal AF with a novel RF ablation microcatheter (Cardima®). Methods: Patients with drug refractory, paroxysmal AF were treated with an RF ablation version of the MAZE procedure placing linear lesions in the right atrium. Patients served as their own controls, establishing a baseline episode frequency in the 30 days prior to treatment. Treatment outcomes were compared to baseline to determine treatment effectiveness. Results: Of 79 subjects who reached 6 months follow up by July 2002, 46.8% reported 100% reduction in symptomatic AF episodes and 84.8% reported $\geq$50% reduction in episode frequency. Subjects also demonstrated clinically significant and statistically significant improvements in quality of life measurements. Conclusion: These results indicate substantial patient benefit from the minimally invasive maze procedure performed with the REVELATION Tx Microcatheter.

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The PREFIB Study: PREvention of Atrial FIBrillation by Rapid Atrial Pacing. Preliminary Results

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Background: Previous studies have compared various atrial pacing rates and pacing sites for preventing atrial fibrillation (AF) recurrences, defined by symptoms or by channels markers and/or by mode switching counters. Counters and markers reliability has never been proven especially in case of muscular noise. New pacemakers provide EGMs storage allowing to optimize the detection of arrhythmia recurrences. Study design: The PREFIB study was designed to assess the time recurrence of AF on two different DDD pacing rates. Thirty patients (pts) with symptomatic recurrent AF or brady-tachycardia syndromes have been implanted with a Guidant Pulsar 1280 pacemaker. In all pts, the atrial lead was positioned in the right atrial appendage. After a 5-days observation period, the DDD pacing rate was randomly programmed at 60 (+ a 15 bpm hysteresis) or at 80 bpm for 12 weeks. Both programmings were crossed over at the end of this fixed period or when symptomatic AF recurred. Antiarrhythmic drug therapy was continued after implantation. AF recurrence was diagnosed by stored EGMs and confirmed by an external loop recorder. Results: Twenty two pts (12 males, 78 ± 7.1 years old) have already completed the study protocol. One pt withdrew for severe heart failure when paced at 80 bpm. For the 21 pts, AF recurred in 12 pts paced at 60 (-15) bpm, after a mean time of 28 days (range 1–64), and in 7 pts paced at 80 bpm, after a mean time of 47 days (range 4–79). Even if this difference is not statistically significant, these results indicate a beneficial trend for faster pacing rates. AF recurrence was asymptomatic in 43% of pts. Conclusion: These preliminary results confirm 1) the beneficial trend of rapid atrial pacing for preventing AF recurrence; 2) the utility of reliable stored EGMs for AF therapeutic management; 3) the need for increasing the EGMs memory size embodied in pacemakers.