Cardiac tests on endurance athletes should include right ventricle

New evidence from a study by researchers in Australia and Belgium has shown that doctors who try to detect arrhythmias in endurance athletes by focusing on the left ventricle of the heart, or on the right ventricle while an athlete is resting, will miss important signs of right ventricular dysfunction that can only be detected during exercise and that could be fatal (La Gerche et al, 2015).

Professor André La Gerche, Head of Sports Cardiology, Baker IDI Heart and Diabetes Institute, Melbourne Australia

The findings have important clinical implications because, at present, routine assessments of athletes with suspected arrhythmias often involve looking at the heart while it is resting, with a focus on the left ventricle.

The researchers tested the performance of the hearts in 17 athletes with right ventricular arrhythmias, eight of whom had an implantable cardiac defibrillator in place to control the rhythm of their hearts, 10 healthy endurance athletes and seven non-athletes. They used both invasive and non-invasive imaging techniques to see the heart at rest and during exercise.

They found that measurements of how well the heart was functioning when the athletes were resting were similar in all three groups, as was left ventricular function during exercise. However, measurements taken while participants were exercising showed changes in right ventricular function in athletes who had arrhythmias compared with the other two groups.

'By measuring the blood pressure in the lungs and the body during exercise we have shown that the right side of the heart has to increase its work more than the left side of the heart. Hence, the right side of the heart is a potential "weak link" in athletes,' explained Professor André La Gerche, associate professor and head of sports cardiology at Baker IDI Heart and Diabetes Institute, Melbourne, Australia, and visiting professor at University Hospitals Leuven, Belgium.

He continued: 'In the normal healthy athletes, the right side of the heart was able to manage the increased work requirements. In the athletes with arrhythmias the right side of the heart was weak during exercise, it could not handle the increase in work and we could detect problems accurately that were not apparent at rest.'

La Gerche A, Claessen G, Dymarkowski S et al (2015) Exercise-induced right ventricular dysfunction is associated with ventricular arrhythmias in endurance athletes. *Eur Heart J* (doi: 10.1093/eurheartj/ehv202)

Out of hospital CPR: mobile phone dispatch of trained laypersons

A blinded, randomized, controlled trial took place to test whether the use of a mobile phone positioning system to dispatch lay responders who are trained in cardiopulmonary resuscitation (CPR) to patients with suspected out-of-hospital cardiac arrest would increase the proportion of cases in which CPR was performed by trained bystanders (Ringh et al, 2015).

A mobile phone positioning system was used to locate trained volunteers who were within 500 m of patients with out-of-hospital cardiac arrest; volunteers were then dispatched to the patients (intervention group) or not (control group).

Overall 9828 lay volunteers who were trained in CPR were recruited. The system was activated in 667 out-of-hospital cardiac arrests: 46% (306 patients) in the intervention group and 54% (361 patients) in the control group. The rate of bystander-initiated CPR was 62% in the intervention group and 48% in the control group (absolute difference for intervention *vs* control 14%, 95% confidence interval 6–21%, $P<0.001$).

Using a mobile phone positioning system to dispatch CPR-trained lay volunteers significantly increased rates of bystander-initiated CPR among persons with out-of-hospital cardiac arrest. The sample size was too small to demonstrate any significant between-group differences in secondary outcomes of return of spontaneous circulation and survival at 1 month.

Ringh M, Rosenqvist M, Hollenberg J et al (2015) Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. *N Engl J Med* **372**: 2316–25 (doi: 10.1056/NEJMoa1406038)

Patients with knee osteoarthritis and poor sleep have worse pain

Patients with knee osteoarthritis who have poor sleep habits display greater central sensitization (Campbell et al, 2015). A case-controlled study showed that patients with osteoarthritis who catastrophize (are consumed by thoughts of pain) had increased central sensitization, associated with greater clinical pain.

The study included 208 participants categorized into four groups: osteoarthritis patients with insomnia, osteoarthritis patients with normal sleep habits, healthy controls with insomnia, and healthy controls without a pain syndrome and normal sleep; 72% of participants were female. Participants completed sleep assessments, psychological and pain evaluations, and sensory testing.

Subjects with knee osteoarthritis and insomnia had the greatest degree of central sensitization compared to the controls. Patients with poor sleep and high catastrophizing scores reported increased levels of central sensitization, and central sensitization was significantly associated with increased clinical pain.

Campbell CM, Buenaver LF, Finan P et al (2015) Sleep, pain catastrophizing and central sensitization in knee osteoarthritis patients with and without insomnia. *Arthritis Care Res* (doi: 10.1002/acr.22609)

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Community-acquired pneumonia increases long-term morbidity and mortality

Having had community-acquired pneumonia greatly increases the risk of long-term morbidity and mortality compared to the general population, according to the longest and largest outcomes study of patients with community-acquired pneumonia reported to date (Eurich et al, 2015).

During a median of 9·8 years of follow up, 2858 patients with community-acquired pneumonia died. There was an absolute risk difference of 30 excess deaths per 1000 patient years of follow up and >50% relative increased rate of mortality among patients with community-acquired pneumonia.

Although patients under 25 years of age with community-acquired pneumonia had the lowest absolute risk difference for mortality, and those over 80 years had the highest absolute risk difference, young adults with community-acquired pneumonia had the worst relative outcomes of all patients with over a 2-fold increased rate of mortality relative to controls.

The mortality rate was significantly higher among patients with community-acquired pneumonia even after including 406 patients who died within 30 days of the index event and excluding a further 248 patients who died within 90 days of admission.

Dr Dean T Eurich, Li Ka Shing Center for Health Research Innovation, University of Alberta, Edmonton, Alberta, Canada

As well as this increased mortality risk, the absolute rates of all-cause hospitalization, emergency department visits and community-acquired pneumonia-related hospital visits were significantly higher in patients with community-acquired pneumonia than controls.

'Future research may help explain the factors underling these increased long-term risks in community-acquired pneumonia patients and inform a treatment approach in these patients,' said Dr Dean Eurich, Associate Professor in the School of Public Health, University of Alberta, Edmonton, Canada. 'Some of these adverse events may be preventable and our results suggest that we have likely underestimated the cost effectiveness, the impact and importance of immunizations that prevent pneumonia.'

Eurich DT, Marrie TJ, Minhas-Sandhu JK, Majumdar SR (2015) Ten year mortality following community acquired pneumonia: a prospective cohort. *Am J Respir Crit Care Med* (doi: 10.1164/rccm.201501-0140OC)

Link between psychotropic drugs and homicide risk

A study analysing the Finnish homicide and prescription drug databases (Tiihonen et al, 2015) found that use of certain drugs that affect the CNS is associated with an increased risk of committing a homicide.

Researchers analysed the pre-crime use of prescription drugs among all persons convicted of a homicide in Finland between 2003 and 2011 – 959 in total. The registers used were the Finnish Homicide Database of the Institute of Criminology and Legal Policy, and the Finnish Prescription Register of the Social Insurance Institution of Finland, Kela.

After confounding factors were controlled for, the results show that the use of antipsychotics was not associated with a significantly increased risk of committing a homicide, whereas the use of antidepressants was associated with a slightly elevated risk (+31%), and the use of benzodiazepines with a significantly elevated risk (+45%).

The study also found that the highest increase in the risk of committing a homicide was associated with opiate painkillers (+92%) and anti-inflammatory painkillers (+206%).

In many cases, very high dose benzodiazepines had been prescribed for a long time. 'Benzodiazepines can weaken impulse control, and ... painkillers affect emotional processing. Caution in prescribing benzodiazepines and strong painkillers to people with a history of substance abuse is advisable,' highlighted lead author Professor Jari Tiihonen, from the Karolinska Institutet, Stockholm, Sweden.

Tiihonen J, Lehti M, Aaltonen M et al (2015) Psychotropic drugs and homicide: a prospective cohort study from Finland. *World Psychiatry* (doi: 10.1002/wps.20220)

Virulent bacteria linked to progression of colon cancer

Changes in the gut bacteria of patients with colon cancer indicate that some virulent bacteria could be linked to the progression of the disease (doi: 10.1186/s13073-015-0177-8). Researchers noted changes in the abundances of helpful, harmless and pathogenic bacteria, including *Fusobacterium* and *Providencia*, the latter for the first time linked to colon cancer.

Action needed to reduce impact of atrial fibrillation

The pan-European 'Future of Anticoagulation' report (www.rand.org/pubs/research_reports/RR1053.html) calls for urgent action to lessen the potential impact of atrial fibrillation in Europe. The prevalence of atrial fibrillation is expected to double in the EU to 17.9 million adults aged over 55 years by 2060.

New antibiotic available to treat acute skin infections

Available in both intravenous and oral formulations, Sivextro (tedizolid phosphate) has been licensed for the treatment of acute bacterial skin and skin structure infections in adults.

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Regional differences in stillbirth and neonatal death rates across the UK

Almost one in every 150 babies born in the UK is stillborn or dies soon after birth. A research team led from the University of Leicester has identified large differences across the UK in the numbers and rates of babies who die, even after taking account of known factors that influence the rate of death such as poverty, mother's age and ethnicity (Manktelow et al, 2015).

A new report by MBRRACE-UK, a team of academics, clinicians and charity representatives (commissioned by the Healthcare Quality Improvement Partnership), has looked behind these figures to try and identify how the situation might be improved. The team has collected data for the 3286 stillbirths and 1436 deaths in the first 4 weeks after birth (neonatal deaths) of babies born at 24 weeks of gestation or more resulting from the 781 929 births in the UK and Crown Dependencies in 2013.

This work adopts a new approach to the analysis of data concerning stillbirths and neonatal deaths for the UK in 2013 including reporting extended perinatal mortality rates (the total of stillbirths plus neonatal deaths).

Pregnancies to women living in areas with the highest levels of poverty in the UK are over 50% more likely to end in stillbirth or neonatal death. Babies of black or black British and Asian or Asian British ethnicity had the highest risk of death with rates of 9.8 and 8.8 per 1000 total births respectively.

The report highlighted differences in the certification of babies born at 22–23 weeks gestational age, incomplete reporting of late fetal loss, and inconsistencies in registration of intrauterine deaths before 24 weeks but which are delivered after 24 weeks. These could have a major influence on national routine statistics, so it is important that these are reported accurately and as completely as possible.

Key findings from the report show significant variation across the UK with the extended perinatal mortality rate ranging from 5.4 to 7.1 per 1000 total births for organizations responsible for commissioning care and similarly for organizations responsible for organizing the delivery of care, even after allowing for factors such as poverty, mother's age and ethnicity.

Professor Elizabeth Draper, Professor of Perinatal and Paediatric Epidemiology, University of Leicester, Leicester

Professor Elizabeth Draper, Professor of Perinatal and Paediatric Epidemiology at the University of Leicester said: ‘This report confirms that the UK performs poorly compared to other European countries of similar economic status particularly Sweden and Norway.’

She continued: ‘We recommend that NHS organizations across the UK and the relevant Royal Colleges establish national aspirational targets for stillbirth, neonatal deaths and extended perinatal deaths. This will enable all services to be assessed against this benchmark in the future in order to work towards achieving similar rates to those of the current best performing countries in Europe.’

Manktelow BM, Smith LK, Evans TA et al on behalf of the MBRRACE-UK collaboration (2015) *Perinatal Mortality Surveillance Report UK Perinatal Deaths for births from January to December 2013.* The Infant Mortality and Morbidity Group, Department of Health Sciences, University of Leicester, Leicester

Scale devised to measure magnitude of clinical benefit from anticancer medicines

ESMO, the European Society for Medical Oncology, has published the ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) (Cherny et al, 2015), a tool to help oncologists evaluate the most effective anticancer medicines for their patients.

‘While it is known that the value of any new treatment is determined by the magnitude of its clinical benefit against its cost, to date there has not been a standard tool for grading such magnitude,’ says Dr Nathan Cherny, Director of the Cancer Pain and Palliative Medicine Service, Department of Medical Oncology, Shaare Zedek Medical Center, Israel, who formulated the idea some years ago.

Dr Nathan Cherny, Director of the Cancer Pain and Palliative Medicine Service, Department of Medical Oncology, Shaare Zedek Medical Center, Israel

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The ESMO-MCBS offers a rational, structured and consistent approach to ‘stratify’ a drug's clinically meaningful benefit.

ESMO intends to apply the scale prospectively to new anticancer drugs that will be approved by the European Medicines Agency. Drugs obtaining the highest scores on the scale will be highlighted in the ESMO Clinical Practice Guidelines, with the hope that they will be rapidly made available by health authorities across the European Union.

The ESMO-MCBS can be used in a range of settings, e.g. in public policy decision making, to develop and/or improve clinical guidelines, and in day-to-day clinical situations.

Cherny NI, Sullivan R, Dafni U et al (2015) A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: The European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol* (doi: 10.1093/annonc/mdv249)

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Clear evidence of link between smoking and prostate cancer

Smoking is a known risk factor for the development of various forms of cancer. However, data regarding the link between smoking and prostate cancer have been contradictory. An international retrospective analysis now provides evidence of a clear link (Rieken et al, 2015).

The analysis was performed to elucidate the association between pretreatment smoking status, cumulative smoking exposure, and time since smoking cessation and the risk of biochemical recurrence of prostate cancer in patients treated with radical prostatectomy.

This retrospective analysis involved 6538 patients with pathologically node-negative prostate cancer treated with radical prostatectomy between 2000 and 2011. Clinicopathological and smoking variables were collected, including smoking status, number of cigarettes per day, duration in years and time since smoking cessation.

The study showed that, following removal of the prostate gland as a treatment for prostate cancer, smokers and ex-smokers had a much higher risk (specifically twice the risk) of recurrence of prostate cancer.

'Our study findings underline the importance of informing a prostate cancer patient about the negative effects of smoking,' commented Dr Shahrokh F Shariat, Principal of the University Clinic of Urology at MedUni Vienn, Vienna, Austria.

Rieken M, Shariat SF, Kluth LA et al (2015) Association of cigarette smoking and smoking cessation with biochemical recurrence of prostate cancer in patients treated with radical prostatectomy. *Eur Urol* (doi: 10.1016/j.eururo.2015.05.038)

Dr Shahrokh F Shariat, Principal, University Clinic of Urology, MedUni Vienn, Vienna, Austria

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Alternatives to parallel group design suggested for trials

New research has the potential to revolutionize global multi-billion pound research activity into the delivery of health services (Hooper and Bourke, 2015).

The work outlines a novel approach to research design which can drastically reduce the number of people involved in some clinical trials, making these trials cheaper and easier to run.

The new technique could be particularly beneficial to trials that involve health interventions at an organizational or institutional level.

The new trial designs are a departure from the classic 'parallel group' approach to running a clinical trial, in which a group of 'control' participants are followed in parallel with a group who receive an experimental treatment. Instead they involve repeated samples of individuals from the same general practice or school, for example, with some assessed before the new treatment is introduced and some after.

This allows researchers to compare individuals' outcomes within an organizational unit as well as between parallel groups of units. If samples are taken in the right pattern the number of individual participants required is reduced.

'Something as unusual-looking as our design shouldn't work, but it does', said Dr Richard Hooper, Senior Lecturer in Medical Statistics at Queen Mary University of London. 'It's a beautiful mathematical idea that has real, practical use in health research which ultimately benefits the users of health services.'

Hooper R, Bourke L (2015) Cluster randomised trials with repeated cross sections: alternatives to parallel group designs. *BMJ* **350**: h2925 (doi: 10.1136/bmj.h2925)

Increased risk of treatment failure for older asthma patients

Older patients with asthma are at increased risk of treatment failure, particularly those patients being treated with inhaled corticosteroids, according to Dunn et al (2015).

Study subjects were drawn from Asthma Clinical Research Network data on patients participating in 10 trials from 1993 to 2003.

Treatment failures were observed in 17.3% of patients 30 years old and above, compared with 10.3% of those under the age of 30 years ($P < 0.001$). Lower lung function measurements and longer duration of asthma were associated with a higher risk of treatment failure.

A greater proportion of patients ≥30 years old receiving controller therapy experienced treatment failures. When stratified by specific treatment, failures increased consistently for every year above the age of 30 years among those patients using inhaled corticosteroids. Patients aged 30 years and older who were treated with inhaled corticosteroids, either alone or in combination, had more than twice the risk of experiencing a treatment failure compared with patients younger than 30 years of age.

'Our novel finding of decreased responsiveness to asthma therapy with increasing age may involve not only biological mechanisms such as differences in the type of airway inflammation in older patients, but may also involve socioeconomic, geographic, or treatment adherence differences between older and younger patients,' said researcher Dr Ryan Dunn, of National Jewish Health in Denver.

Dunn RM, Lehman E, Chinchilli VM et al; NHLBI Asthma Clinical Research Network (2015) Impact of age and gender on response to asthma therapy. *Am J Respir Crit Care Med* (doi: 10.1164/rccm.201503-0426OC)

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