Institution: Buckinghamshire New University

Unit of Assessment: Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study: Cardiac power output as a novel approach to functional measurement in cardiovascular health

1. Summary of the impact

The research team at Bucks New University has provided the groundwork for a number of applications to use cardiac power output as a novel functional measurement in the clinical evaluation of patients with heart failure and other related diseases. It involved validating the measure, assessing its reliability and applying it to a group of patients with end-stage heart failure. The success of this procedure is now evidenced by the number of national and international clinical centres adopting cardiac power output as a key functional measurement.

2. Underpinning research

The research into cardiac power output (CPO) was co-ordinated by Professor Brodie of Bucks New University during the period 2004 to 2012. The team included Professor Sir Magdi Yacoub, (Heart Science Centre, Harefield Hospital), Professor Emma Birks, (currently Director, Heart Failure, Transplant and Mechanical Support Programme, University of Louisville), Dr Richard Grocott-Mason (Consultant Cardiologist, Hillingdon Hospital), Dr Djordje Jakovljevic (currently Senior Research Associate, Newcastle University) and a small group of PhD students.

The initial focus of the research was to explore the reliability and validity of CPO as an integral measure of both flow and pressure generating capacity of the heart. This involved a comparison of different rebreathing methods and resulted in the conclusion that inert gas rebreathing measured cardiac output more precisely than the alternative carbon dioxide rebreathing methods (1). As the target patient group was those with chronic heart failure, it was essential to explore the reproducibility of CPO in such groups and this was established with a low coefficient of variation. The outcome was a clear demonstration that CPO was an excellent prognostic marker and was subsequently strongly advised in the assessment of patients undergoing cardiopulmonary exercise testing. The process of cardiac rehabilitation can include both aerobic and resistance training and it was important to determine which was the most effective in improving cardiac function using CPO as the main determinant. Our work (3) demonstrated that aerobic exercise training increased the maximal flow-generating capacity of the heart and delayed anaerobic metabolism in patients with stable chronic heart failure.

Much of our work was in association with the Magdi Yacoub Institute involving patients on the 'Bridge to Recovery' programme at Harefield Hospital. These patients were initially in end-stage heart failure, awaiting heart transplantation, but as a result of the programme, involving the use of a left ventricular assist device (LVAD) many recovered sufficiently to avoid transplantation. One important contribution to the programme was our investigation into the impact of acute reduction of continuous-flow LVAD support on cardiac and exercise performance (4). We showed for the first time that the LVAD can confer both resting and peak cardiac functional benefits to patients with end-stage heart failure. We also showed that exercise-derived prognostic indicators demonstrated a limited capacity in reflecting cardiac pumping capability in patients treated with LVADs. Thus the interpretation of cardiac organ function would benefit substantially by the inclusion of CPO.

As patients responded positively to the Harefield Protocol, a number had their LVADs removed (explanted) and it was important to assess the extent of the protocol by using CPO as a direct

measure of overall cardiac function. We compared those patients still using the LVAD, those whose LVAD had been explanted and those with moderate to severe heart failure. It was concluded that peak CPO a) differentiates well during cardiac restoration using LVADs and emphasizes the benefits of this therapy, and b) can guide the management of patients with LVADs.

3. References to the research

The following six key references were all published in peer reviewed journals:

1. Jakovljevic DG, Nunan D, Donovan g, Hodges LD, Sandercock GR, Brodie DA, Comparison of cardiac output determined by different rebreathing methods at rest and at peak exercise. Eur. J. Appl. Physiol 2008, Mar 102(5) 593-9
2. Jakovljevic DG, Seferovic PM, Nunan D, Donovan G, Trenell MI, Grocott-Mason R, Brodie DA, Reproducibility of cardiac power output and other cardiopulmonary exercise indices in patients with chronic heart failure. Clin Sci (London) 2012 Feb 122 (4) 175-181
3. Jakovljevic DG, Nunan D, Donovan G, McDonagh S, Trenell MI, Grocott-Mason R, Brodie DA, The effect of aerobic versus resistance exercise training on peak cardiac power output and physical functional capacity in patients with chronic heart failure. Int J. Cardiol. 2010, Dec 3 145(3) 526-8
4. Jakovljevic DG, George RS, Nunan D, Donovan G, Bougard RS, Yacoub MH, Birks EJ, Brodie DA, The impact of acute reduction of continuous-flow left ventricular assist device support on cardiac and exercise performance. Heart 210 Sept 96 (17) 1390-5
5. Jakovljevic DG, Birks EJ, George, RS, Trenell MI, Seferovic PM, Yacoub MH, Brodie DA, Relationship between peak cardiac pumping capability and selected exercise- derived prognostic indicators in patients treated with left ventricular assist devices. Eur J. Heart Fail. 2011 Sept 13 (9) 992-9
6. Jakovljevic DG, George, RS, Donovan G, Nunan D, Henderson k, Bougard RS, Yacoub MH, Birks EJ, Brodie DA, Comparison of cardiac power output and exercise performance in patients with left ventricular assist devices, explanted (recovered) patients, and those with moderate to severe heart failure. Am J. Cardiol. 2010, June 15, 105 (12), 1780-5

4. Details of the impact

Research work on the failing heart has focused on its anatomy, physiology and pathophysiology both at macro and micro-cellular levels. Imaging techniques and advanced genetic, structural and pharmacological aspects all aid in diagnosis and prognosis. In spite of this, relatively little work has focused on the heart's total functional capacity, often using analogues such as oxygen uptake or partial substitutes such as ejection fraction or cardiac output. We chose to research cardiac power output, which describes the function of the heart in terms of both flow and pressure generating capacities. The initial contribution was to provide solid evidence for the reliability of the measure in the target population of patients with heart failure and to explore its face validity in comparison with alternative methods of measurement. This basic research then led on to a series of applied investigations involving patients undergoing cardiac rehabilitation and those participating in the world's famous and most successful Harefield 'Bridge to Recovery' protocol, prior to heart transplantation. The outcome of the cardiac rehabilitation programme provided further substantial evidence for the benefit of aerobic training and has impacted on the policies of the British Association for Cardiovascular Prevention and Rehabilitation (BACPR). Professor Brodie was at the time a Council member of the BACPR and was involved in framing the policies and core components of the Association in terms of exercise modalities.

We introduced three new diagnostic parameters to the existing protocol at Harefield, which at that

time was heavily reliant on clinical measures and oxygen consumption during progressive exercise. The three we introduced were heart rate recovery, heart rate variability and cardiac power output, the latter being the focus of this impact case study. Cardiac power output was fully integrated into the diagnostic element of the Harefield protocol during the time of our studies, providing for the first time a true measure of cardiac functional capacity. At this time, the team led by Professor Birks, Professor Brodie and Professor Sir Magdi Yacoub were investigating the impact of acute and chronic reduction of continuous flow LVAD support. Cardiac power output contributed substantially to the knowledge base on reduced LVAD support and provided a solid base for the future management of patients on LVADs. The impact is that centres in the UK using LVADs in clinical practice, are now establishing similar procedures in recovery evaluation of LVAD patients. The impact of our work on cardiac power output has yet to impact on national policy, essentially because relatively few centres in the UK utilize the LVAD implantation procedure. However centres at Leeds and Newcastle do now use cardiac power output routinely in the management of heart failure patients. .

Following the original research undertaken at Bucks New University, the work has extended to The Neurology Department at Newcastle Royal Victoria Infirmary (2). The Neurology Department is the national centre for rare, inherited mitochondrial diseases directed by Professor Douglas Turnbull. In addition to numerous clinical examinations that patients with mitochondrial diseases undergo during their appointment, many of them undergo maximal graded cardiopulmonary exercise testing with non-invasive gas exchange and central haemodynamic measurements such as cardiac output and cardiac power output. This examination helps clinicians to identify causes of exercise intolerance which is a clinical hallmark of patients with mitochondrial disorders. It further helps clinicians to manage disease and advise appropriate pharmacological and physiological therapies known to improve clinical symptoms and exercise intolerance. Our work has directly impacted on the Institute for Ageing and Health at Newcastle University, Europe's largest Institute for Ageing. This Institute now has a number of clinical groups studying the heart's functional capacity using CPO and adopting the procedures we developed to measure the limitations to everyday functioning and exercise, non-invasively. These clinical groups include metabolic diseases (e.g. type 2 diabetes, non-alcoholic liver disease, biliary cirrhosis), neuromuscular disorders (e.g. mitochondrial diseases) and ageing and age related diseases (e.g. Parkinson's) (4)

Further evidence for the impact of our work on CPO is the adoption of the procedure at two international hospitals and research centres, both at the personal invitation of Prof Sir Magdi Yacoub. Dr Jakovljevic (4) who worked on CPO at Bucks New University, has been invited to establish the clinical investigation laboratory, using CPO as a routine procedure in the assessment of cardiac patients undergoing open heart surgery at the Magdi Yacoub Heart Foundation supported Aswan Heart Centre in Egypt (5). Cardiopulmonary exercise testing laboratory with non-invasive central haemodynamic measurements was established in October 2012. Since then, all patients who are considered for cardiac surgery undergo exercise testing with cardiac output and cardiac power output reported in conjunction with cardiorespiratory fitness. This helps clinical teams to define cardiac performance and functional capacity of patients and help further with risk stratification. CPO measurement is also used to evaluate patients' recovery following surgery. Dr Jakovljevic will soon be establishing a similar clinical laboratory at the Sidra Medical and Research Center, Doha, Qatar (6). Thus the benefit of our work is multinational and will impact on patients both in the UK and Middle East.

5. Sources to corroborate the impact

1. Consultant Cardiologist and Medical Director, The Hillingdon Hospital NHS Foundation Trust.

2. Consultant Neurologist, Royal Victoria Infirmary, Newcastle upon Tyne

3. http://www.ncl.ac.uk/biomedicine/research/brc/

4. Senior Research Associate (Clinical Applied Physiology), Newcastle University Medical School

5. http://www.aswanheartcentre.com/

6. http://sidra.org/introduction/