**Institution:** University of Bristol

**Unit of Assessment:** 1 – Clinical Medicine

**Title of case study:** Lower risks to patients, advances in international practice and substantial resource savings result from 'beating heart' off-pump coronary artery bypass surgery.

**1. Summary of the impact** (indicative maximum 100 words)

University of Bristol researchers at the Bristol Heart Institute (BHI) have pioneered the development and clinical take-up of the novel technique of off-pump coronary artery bypass (OPCAB) surgery. Over ten clinical trials and several large cohort analyses have assessed the impact of this technique on elective and high-risk patients. The results have shown that it is as safe as the conventional coronary artery bypass grafting (CABG) technique that uses a cardiopulmonary bypass pump and cardioplegic arrest. Most importantly, however, OPCAB significantly reduces the risk of post-operative complications, and reduces morbidity and mortality. It also uses less hospital resources, reducing time in intensive care and length of hospital stay. In 2011 (the last year for which data are available), 20% of CABG operations in the UK were carried out with the OPCAB technique and it has had significant take-up overseas (for example, 18% of CABG operations in the US and 21% in the EU in 2010). NICE has recommended the safety and efficacy of OPCAB surgery.

**2. Underpinning research** (indicative maximum 500 words)

Conventional coronary artery bypass grafting (CABG) surgery in an increasingly high-risk population (caused by increasing age, smoking, diabetes, hypertension and high cholesterol) involves stopping the heart (cardioplegic arrest, CA) and the use of a cardiopulmonary bypass pump (CPB). The use of CA and CPB in these patients is associated with significant in-hospital mortality and morbidity due to its non-physiological nature. To overcome these problems, researchers from the University of Bristol at the Bristol Heart Institute (BHI) have pioneered the novel and alternative technique of off-pump coronary artery bypass surgery (OPCAB), avoiding the use of both CA and CPB. The BHI is an internationally recognised centre of excellence for performing translational cardiovascular research that takes basic science discoveries to the clinic.

OPCAB has been developed and validated at the BHI since 1997 by a team led by Professor Gianni Angelini, British Heart Foundation Professor of Cardiac Surgery, and Professor Raimondo Ascione, Professor of Cardiac Surgery & Translational Research (Clinical Research Fellow in Cardiac Surgery at the BHI in 1997). Other key research team members include Professor Barnaby Reeves (Professor of Health Services Research and Honorary Senior Lecturer in Epidemiology in 2002 when he joined the BHI) and Mr Alan Bryan (Consultant Cardiac Surgeon and responsible for the BHI data registry since 1998). The development and validation process has involved over ten trials and several large cohort analyses from the BHI data registry.

Preliminary work between 1997 and 1998 focused on the development of a reproducible surgical technique with use of locally developed tools. The established technique was reported in 2001.[1] A series of small trials assessed its impact on subsystem organ function in 1997-98, including myocardial,[2] renal,[3] respiratory, cerebral and inflammation. Larger trials followed (Beating Heart Against Cardioplegic Arrest Studies 1&2) in 1999-2001,[4, 5] with follow-up in 2003 [6] and 2008, assessing late symptoms and graft patency rate. In addition, case cohort studies (2001-2006) assessed the impact on in-hospital and mid-term clinical end-points, including mortality in elective and high-risk patients. A further trial focused for the first time on cerebral and retinal micro-embolisation.[7] The BHI conducted and published the world's first randomised study on OPCAB surgery.[2] No other centres were rigorously validating the same approach in parallel, as is evident from the absence of concomitant randomised trials published by others. Thus the procedure was validated through rigorous studies from 1997 to 2008, showing that patients benefited directly in terms of reductions in in-hospital morbidity,[5] blood loss, transfusion requirement,[4] chest infection, inotropic support,[5] arrhythmias,[a] cerebral embolisation and renal injury [3] when

compared with conventional technique in elective patients, without affecting mid- and long-term benefit.[6] The research has been funded to a total of approximately £3m. The first two funding grants were awarded in 1997 and 2001.[7, 8]

**3. References to the research** (indicative maximum of six references)

**Peer-reviewed journal publications**


[1] Watters MP, Ascione R, Ryder IG, Ciulli F, Pitsis AA, Angelini GD. Haemodynamic changes during beating heart coronary surgery with the 'Bristol Technique'. Eur J Cardiothorac Surg. 2001 Jan;19(1):34-40. DOI: 10.1016/S1010-7940(00)00603-5

[2] R Ascione, CT Lloyd, WJ Gomes, M Caputo, AJ Bryan, GD Angelini. Beating versus arrested heart revascularization: evaluation of myocardial function in a prospective randomised study. Eur J Cardio-Thoracic Surg; 1999;15:685-690. DOI: 10.1016/S1010-7940(99)00072-X

[3] Ascione R, Lloyd CT, Underwood MJ, Gomes WJ, Angelini GD. On-pump versus off-pump coronary revascularization: evaluation of renal function. Ann Thorac Surg. 1999 Aug;68(2):493-8. DOI: 10.1016/S0003-4975(99)00566-4

[4] R Ascione, S Williams, CT Lloyd, T Soondaramorthi, AA Pitsis, GD Angelini. Reduced postoperative blood loss and transfusion requirement after beating-heart coronary operations: a prospective randomised study. J Thorac Cardiovasc Surg 2001;121:689-96. DOI: 10.1067/mtc.2001.112823

[5] GD Angelini, FC Taylor, BC Reeves, R Ascione. Early and mid-term outcome after off-pump and on-pump surgery in Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. Lancet 2002;359:1194-99. DOI: 10.1016/S0140-6736(02)08216-8

[6] Ascione R, Reeves BC, Seehra H, Taylor FC, Angelini GD. Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): quality of life at mid-term follow-up in two randomised controlled trials. Eur Heart J 2004;25:765-70. DOI: 10.1016/j.ehj.2003.11.015


**Peer reviewed grants**


[7] Angelini GD. Coronary artery revascularisation without cardiopulmonary bypass: a prospective randomised controlled study. 1997-1999. Sir Siegmund Warburg Voluntary Settlement £69,876

[8] Ascione R, Bryan AJ, Angelini GD. On pump versus off pump coronary surgery: evaluation of small intestinal, pancreatic and liver function. 2001-2002. BHF £53,610


**4. Details of the impact** (indicative maximum 750 words)

**Impact on patients**

As a result of the trials and cohort studies, the BHI team demonstrated that the technique they developed is as safe as conventional CABG using a cardiopulmonary bypass pump.[1-6] A 2010 study sought to compare off- and on-pump surgery through a systematic review and meta-analysis of propensity score analyses.[a] The estimated overall odds ratio was less than 1 for all outcomes, favouring off-pump surgery. This benefit was statistically significant for mortality (odds ratio, 0.69; 95% confidence interval (CI) 0.60-0.75), stroke, renal failure, red blood cell transfusion, wound infection, prolonged ventilation, inotropic support, and intra-aortic balloon pump support. The study found off-pump surgery superior to on-pump surgery in all of the assessed short-term outcomes. This advantage was statistically significant and clinically important for most outcomes, including mortality. These results agree with previous systematic reviews of randomised and non-randomised trials. A 2009 study analysed the risk reduction of cardiopulmonary bypass complications between on-pump and off-pump coronary artery bypass grafting in high-risk patients. In the intention to treat analysis, the rate of the composite primary end point was significantly lower in the off-pump group (5.8% versus 13.3%). The risk of experiencing the primary end point was significantly greater for the on-pump group (unadjusted odds ratio, 2.51; 95% CI, 1.23-5.10; P = 0.011; adjusted odds ratio, 3.07; 95% CI, 1.32-7.14; P = 0.009). The study concluded that OPCAB reduces early mortality and morbidity in high-risk patients.[b]

A 2013 study queried the Society of Thoracic Surgeons National Cardiac Database for all patients undergoing non-emergency, isolated coronary artery bypass from 2005 to 2010, who had Predicted Risk of Mortality scores and participant/surgeon identifiers. Of these 876,081 patients

("all sites"), 210,469 underwent surgery at participant sites that had performed more than 300 off-pump and 300 on-pump coronary artery bypass operations during the 6-year study period ("high-volume sites"). A number of outcomes were analysed with conditional logistic models for all sites and for high-volume sites, stratified by participant centre and surgeon, and adjusted for 30 variables that comprise the Society of Thoracic Surgeons CABG risk models. In this analysis, OPCAB was associated with reduced risk of death, stroke, acute renal failure, mortality or morbidity, and prolonged length of stay after adjustment for 30 patient risk factors and stratifying for both centre and surgeon identity. OPCAB had a significantly greater reduction in these adverse events in patients with higher patient reported outcome scores. The benefit of OPCAB, therefore, may be more apparent in high-risk patients.[c] The European Association for Cardio-Thoracic Surgery (EACTS) Adult Cardiac Surgical Database Report 2010, contains information on over one million patients undergoing adult cardiac surgery in 366 hospitals in 29 countries across Europe and China. It reports an associated mortality rate of 1.4% (OPCAB) versus 2.9%.[d]

**Impact on international practice**

Many surgeons had previously been reluctant to take up OPCAB because of concerns that the technique required surgery on the beating heart, potentially causing late blockage of the grafted arteries. The literature on graft patency from randomised controlled trials of OPCAB versus CABG-CPB is inconsistent, and studies conducted in 2005-6 reported findings for only relatively short durations of follow-up [e]. To address these concerns, the BHI has conducted and published in 2009 the longest follow-up study in the world directly comparing the two techniques. Participants in two randomised trials previously undertaken at the BHI comparing OPCAB and CABG-CPB were followed up for six to eight years after surgery. The findings conclusively demonstrated that the likelihood of graft occlusion was no different between OPCAB (10.6%) and CABG-CPB (11.0%) [f].

These data were presented and discussed at the 88th Annual Meeting of The American Association for Thoracic Surgery in May 2008 (the world's largest gathering of cardiac surgeons). The discussion clearly demonstrated that in Japan, surgeons have adopted this technique for about 60% of patients undergoing CABG, and in the Japan's National Cardiovascular Centre 98% of CABG procedures have been performed using OPCAB. Currently, it is estimated that 20-25% of CABG operations worldwide are carried out with the OPCAB technique. The National Adult Cardiac Surgery Audit 2010-11 [g] reported that more than 26,000 CABG operations in the UK in 2011 used OPCAB (20% of all such operations). In the US, 18% of CABG operations are carried out with the OPCAB technique as of 2010.[h] The EACTS Adult Cardiac Surgical Database Report 2010 notes that in 29 countries across Europe and China, "21% of those patients undergoing coronary artery surgery in which the technique is described had off-pump surgery. This varies between countries from 0.8% up to 91.4%.".[d] The report details that 61% of CABG procedures have been performed using the OPCAB in China.[d] Of the 95,000 CABG performed per year in India, 30% had off-pump surgery.[i] OPCAB surgery is now routine practice for five out of the seven Consultant Cardiac Surgeons at the BHI Hospital, constituting >95% of their coronary surgical practice. The total number of OPCAB cases at the BHI has gone from <5% (25-30 cases per year) in 1995 to >75% (>750 cases per year; >8000 cases in total) in 2011.[j]

NICE has recommended the safety and efficacy of OPCAB surgery, through interventional procedure guidance noting that, "Current evidence on the safety and efficacy of off-pump coronary artery bypass grafting is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit".[k] An effective programme of training in OPCAB surgery has been implemented at the BHI.[k] Once surgeons are trained and accustomed to do it, they are reluctant to go back to CABG-CPB because they are more comfortable with the OPCAB technique and its reduction in early post-operative morbidity and use of resources. Consultants trained in beating heart coronary surgery at the BHI and now performing this surgery elsewhere include six in the UK outside of Bristol, and the following consultants internationally: Mr A Gosh, Consultant Cardiac Surgeon, Kolkata, India; Mr P Narayan, Consultant Cardiac Surgeon, Kolkata, India; Professor W Gomes, Professor of Cardiac Surgery, San Paolo, Brazil; Mr A Pitsis, Consultant Cardiac Surgeon, Athens, Greece; Mr W Dihmis, Consultant Cardiac Surgeon, Amman, Jordan; Mr B Izzat, Professor of Cardiac Surgery, Damascus, Syria.

**Impact on resources**

The OPCAB technique has had a profound impact on hospital resources and cost, with a 25% saving per patient. A 2003 BHI study recorded a dramatic reduction in intensive care unit and hospital stay [5], as shown in the following table:

| | CABG | OPCAB |
|---|---|---|
| ICU stay (>1 day) | 22% | 7% |
| Hospital stay (>7 days) | 29% | 15% |

The reduction in hospital stay was confirmed in 2013 in a study that reported an odds ratio of 0.77 for postoperative length of stay across all of the sites analysed (adjusted by patient).[c] A 2005 meta-analysis examined five studies which have reported on the in-hospital costs and each of them showed OPCAB to be less costly than CABG, with an odds ratio of 0.77 across all of the sites analysed (adjusted by patient).[e] The study included a collation of all the hospital costs from the date of surgery to the date of discharge including all patient services and supplies. The study calculated an average cost per patient of $23,053 for CABG and $17,780 for OPCAB. Across the 26,000 operations in the UK in 2011 using OPCAB, this equates to a saving of US$137 million.

**5. Sources to corroborate the impact** (indicative maximum of 10 references)


[a] Kuss O, von Salviati B, Borgermann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. J Thorac Cardiovasc Surg 2010;140;829-35. DOI: 10.1016/j.jtcvs.2009.12.022. Corroborates superiority of off-pump to on-pump in short term outcomes including stroke, renal failure and mortality.

[b] Puskas JD, Thourani VH, Kilgo P, et al. Off-pump coronary artery bypass disproportionately benefits high-risk patients. Ann Thorac Surg 2009;88:1142-7. DOI: 10.1016/j.athoracsur.2009.04.135. Corroborates that OPCAB reduces early mortality and morbidity.

[c] Polomsky M, He X, O'Brien Sm, Puskas JD. Outcomes of off-pump versus on-pump coronary artery bypass grafting: Impact of preoperative risk. J Thorac Cardiovasc Surg 2013;145;1193-1198. DOI: 10.1016/j.jtcvs.2013.02.002. Corroborates that OPCAB was associated with reduced risk of death, stroke, renal failure, mortality or morbidity, and prolonged length of stay.

[d] EACTS Adult Cardiac Surgical Database Report, 2010. Corroborates use of OPCAB across Europe and China.

[e] Wijeysundera DN, Beattie WS, Djaiani G, Rao V, Borger MA, Karkouti K, et al. Off pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. J Am Coll Cardiol. 2005;46:872-82. DOI: 10.1016/j.jacc.2005.05.064. Corroborates reduced costs of OPCAB.

[f] GD. Angelini, L Culliford, D Smith, M Hamilton, G Murphy, R Ascione, et al. Effects of on- and off-pump coronary artery surgery on graft patency, survival and quality of life: long term follow-up of two randomised controlled trials. J Thorac Cardiovasc Surg 2009;137:295-303. DOI: 10.1016/j.jtcvs.2008.09.046. Corroborates that OPCAB does not cause long term blockage of the grafted arteries.

[g] 6th National Adult Cardiac Surgical Database Report-Blue Book, http://www.scts.org/. Corroborates number of OPCAB surgeries performed in UK.

[h] STS Database Registry 2010, http://www.sts.org/quality-research-patient-safety/sts-public-reporting-online. Corroborates number of CABG surgeries performed in US.

[i] Senior Vice Chairman, Medica Superspecialty Hospital Kolkata. India. Corroborates number of OPCAB surgeries performed in India.

[j] BHI Adult Cardiac Surgery Activity Audit Report 2010-11. Corroborates number of OPCAB surgeries performed at BHI hospital.

[k] NICE. 'Off-pump Coronary Artery Bypass Grafting'. NICE interventional procedure guidance 377. January 2011. www.nice.org.uk/nicemedia/live/11034/52580/52580.pdf. Corroborates NICE recommendation of OPCAB surgery.

[l] M Murzi, M Caputo, G Aresu, S Duggan, GD. Angelini. Training residents in off-pump coronary artery bypass surgery: A 14-year experience. J Thorac Cardiovasc Surg 2012;143:1247-53. DOI: 10.1016/j.jtcvs.2011.09.049.