NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of off-pump coronary artery bypass grafting

Off-pump coronary artery bypass grafting

Coronary artery disease (also called coronary heart disease or ischaemic heart disease) happens when the build-up of a fatty substance narrows or blocks the arteries restricting supply of blood to the heart muscle, which may cause chest pain (angina) or a heart attack.

Coronary artery bypass grafting aims to improve the flow of blood to the heart muscle. The surgeon uses a healthy blood vessel, usually taken from the chest or the leg, and attaches it on the heart muscle so that blood can get round ('bypass') the affected part of the coronary artery.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2010.

Procedure name

- Off-pump coronary artery bypass grafting

Specialty societies

- Society for Cardiothoracic Surgery in Great Britain and Ireland

Description

Indications and current treatment

Coronary artery disease (CAD) (single or multiple vessel) for which surgical revascularisation is indicated is characterised by the progressive accumulation of atherosclerotic deposits within the coronary arteries. The key clinical manifestations are angina and myocardial infarction (the latter occurs when a coronary artery is completely blocked by thrombus). Conservative management aims to control angina and lead to the secondary prevention of myocardial infarction using cholesterol-lowering medications, antiplatelet treatment, anti-hypertensive therapy and smoking cessation/cardiac rehabilitation as appropriate. In addition, some patients can benefit from revascularisation of ischaemic myocardial sections, either through percutaneous transluminal coronary angioplasty, with or without stenting, or by coronary artery bypass graft (CABG) surgery.

CAB graft surgery aims to increase blood flow to ischaemic parts of the heart muscle by the construction of bypass grafts beyond narrowed or occluded coronary arteries. This is achieved by surgically creating an alternative conduit around the blocked arterial section using an arterial or venous graft. The procedure is most often performed ‘on pump’ while circulation is maintained extra-corporeally using a cardiopulmonary bypass machine, and on an arrested (non-beating) heart (cardioplegia).

What the procedure involves

Off-pump CABG is considered a less invasive form of CABG by avoiding the potential hazards of cardiopulmonary bypass, mainly in relation to risk of stroke.

With the patient under general anaesthesia, and following a thoracotomy, the heart is displaced and snares are placed around target coronary arteries to occlude them while the bypass grafts are sutured in place. An immobilising device is used to minimise movement of the beating heart while the anastomoses are performed. Donor vessel harvesting is performed in the standard way.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to off-pump coronary artery bypass. Searches were conducted of the following databases, covering the period from their commencement to 9 December 2009 and updated to 1 October 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies

identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients requiring coronary artery bypass grafting.
Intervention/test	Off-pump coronary artery bypass grafting.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 531,000 patients from two systematic reviews[1,2], one randomised controlled trial[3], three non-randomised controlled studies[4,5,6], one national registry[8], one case series[9], and one case report[7].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on off-pump coronary artery bypass grafting

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings	Comments
Møller C H (2008)[1] **Meta analysis of RTC's** International studies Recruitment period: Not reported. (Search to June 2007) Study population: studies comparing off-pump CABG to on-pump CABG with cardioplegia. n = **5537** (overall numbers in each group not reported) Age: 63 years (mean) Sex: 22% female Patient selection criteria: Not reported Studies included: 66 RCTs. For details please see original study report Technique: Off-pump CABG with any type of stabilisation system **Follow-up: Range of mean/medians from 1 day to 5 years** Conflict of interest/source of funding: not reported	The timing of the assessment of follow-up outcomes varies between 1 day and 5 years. Therefore, it was not possible to separate post-operative/within 30 day-outcomes (safety) and subsequent outcomes (efficacy). Consequently, efficacy and safety outcomes are reported together. Number of patients analysed: **number of patients included in each analysis is reported separately but number in each study group not reported.** **Mortality (n = 5202) (2619 off pump)** There was no statistically significant difference between off-pump and on-pump CABG in pooled mortality rate, relative risk 0.98 (95% CI 0.66 to 1.44). No significant heterogeneity. Length of follow-up not reported. **Myocardial infarction (n = 4303) (2157 off pump)** There was no statistically significant difference between off-pump and on-pump CABG in pooled MI rate, relative risk 0.95 (95% CI 0.65 to 1.37). No significant heterogeneity. Length of follow-up not reported. **Stroke (n = 4535) (2269 off pump)** There was a significantly lower rate of stroke following off-pump CABG than on-pump CABG, relative risk 0.53 (95% CI 0.31 to 0.91) (p = 0.02). Off-pump stroke event rate 0.7% (17/2269), on pump 1.7% (38/2266). No significant heterogeneity. Length of follow-up not reported. However, when studies with zero events were included in analysis, the difference was no longer significant. **Atrial fibrillation (n = 3634) (1843 off pump)** There was a significantly lower rate of atrial fibrillation following off-pump CABG than on-pump CABG, relative risk 0.69 (95% confidence interval 0.57 to 0.83) (measurement of significance not reported). There was a moderate degree of heterogeneity between study results. **Repeat revascularisation (n = 2215) (1106 off pump)** There was no statistically significant difference between off-pump and on-pump CABG in pooled revascularisation rate, relative risk 1.35 (95% confidence interval 0.83 to 2.18). Length of follow up not reported.	**Follow-up issues**: The conversion rate to on-pump CABG was 5% (range 0 to 20%). Primary studies reported intention to treat or it was calculated where possible. Otherwise sensitivity analysis undertaken. **Study design issues**: Thorough database search and cross referencing. No language restrictions. Search strategy not reported. Duplicate assessment of study eligibility and quality. Sensitivity analysis undertaken on basis of study quality 1050 patients came from 5 trials with a low-bias risk. Publication bias assessed. Random effects model for pooling of results and heterogeneity tested for. **Study population issues**: Baseline patient characteristics not reported. It is assumed that it was similar across treatment groups in the primary studies included. 34 of trials analysed exclude patients with ejection fraction < 0.30. **Other issues**: Subgroup analysis showed no effect on off-pump technique or heparin dose on any outcome.

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings	Comments
Wijeysundera D N (2005)[2] **Meta analysis** International studies Recruitment period: Not reported. (Search to June 2004) Study population: studies comparing off-pump CABG to on-pump CABG **n = 297,000** Age: not reported Sex: not reported Patient selection criteria: Not reported Studies included: 37 RCTs and 22 non-RCTs. For details please see original study report Technique: Off-pump CABG not otherwise described vs on-pump CABG **Follow-up: not reported** Conflict of interest/source of funding: not reported.	Except for ≤ 30-day mortality (safety outcome) the timing of the assessment of other follow-up outcomes varies between 1 day and 5 years. Therefore, it was not possible to separate outcomes into post-operative/within 30 days (safety) and subsequent outcomes (efficacy). Consequently, efficacy and safety outcomes are reported together. Number of patients analysed: **number of patients included in each analysis is reported separately but number in each study group not reported.** The following table summarises results from non-randomised controlled trials (22 studies, 293,617 patients) **Odds ratio < 1 favour off pump vs on pump** Outcome (patients included in analysis) | Odds ratio (95% CI) | p Mortality ≤ 30 day (268,547) | 0.72 (0.66 to 0.78) | < 0.00001 Stroke (290,621) | 0.62 (0.55□to 0.69) | < □□00001 MI (24,796) | 0.66 (0.50 to 0.88) | 0.004 Atrial fibrillation (20,664) | 0.87 (0.74 to 0.82) | < 0.0001 Low cardiac output (9193) | 0.62 (0.47 to 0.82) | 0.0009 Re-op□ration for bleeding (31,964) | 0.75 (0.41 to 1.38) | 0.36* Acute renal failure (237,990) | 0.54 (0.39 to 0.77) | 0.0006* Blood transfusion (1832) | 0.62 (0.50 to 0.76) | < 0.00001 **Long-term outcomes (1 to 2 years)** Mortality (1,832) | 1.01 (0.74 to 1.40) | 0.93 MI (1,832) | 0.91 (0.55 to 1.49) | 0.70 Revascularisation (1832) | 1.35 (0.76 to 2.39) | 0.31 * Significant heterogeneity between studies	**Follow-up issues**: Analysis on intention to treat basis. **Study design issues**: Thorough database search and cross referencing. No language restrictions. Duplicate assessment of study eligibility and quality. Pooling using the fixed-effect model unless significant heterogeneity identified, in which case random effects model used. **Study population issues**: None. Outcomes reported from non-RCTs might be subject to selection bias. **Other issues**: All but three of the RCTs included in this meta-analysis (which report on non-clinical outcomes only) are reported in the meta-analysis by Møller (2008), so only results from meta analysis of the non-RCTs are extracted here. Authors note that RCTs did not show off-pump CABG to reduce mortality, while in contrast, in observational studies there was a statistically significant benefit with off-pump CABG.

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings		Comments
Shroyer A L (2009)[3] ROOBY trial **Randomised controlled trial** USA Recruitment period: 2002 to 2008. Study population: patients scheduled for urgent or elective CABG procedures. Urgent surgery required in 15% of patients. **n = 2203 (1104 off pump vs 1099 on pump)** Age: 63 years (mean) Sex: 1% female Patient selection criteria: patients without significant valve disease, small target vessels, diffuse coronary disease, or at extremely high risk of an adverse event. Technique: standard median sternotomy for both groups. Off-pump CABG using various stabilisers vs on-pump CABG **Follow-up: 1 year (median)** Conflict of interest/source of funding:	Number of patients analysed: **n = 2203 (1104 off pump vs 1099 on pump)** ***Number of grafts compared with planned number of grafts*** The proportion of patients who had fewer grafts during the procedure than planned at baseline was significantly higher in the off-pump group (17.8%) than in the on-pump group (11.1%) ($p < 0.001$) (absolute figures not reported). ***Graft patency*** 62.2% (1371/2203) of patients who were alive underwent follow up angiogram assessment. Overall, significantly fewer grafts were patent in the off-pump group 82.6% (1650/1998) than in the on-pump group 87.8% (1839/2095) at 12 months follow up ($p < 0.001$). ***Neuropsychological outcomes*** 73.9% (1331/1801) of patients who underwent baseline assessment had testing at 12 months follow up. Patients in the off-pump group showed a significantly better change in score in the clock-drawing test (not otherwise described) (0.26 ± 0.99) than those in the on-pump group (0.09 ± 0.90) ($p = 0.001$). There was no significant difference between the groups in any other neuropsychological test. ***Operative characteristics*** Outcome / Off pump / On pump / p Surgical time (hours) / 4.5 ± 1.4 / 4.4 ± 1.3 / 0.05 Length of stay (days) / 8.2 ± 8.8 / 7.8 ± 6.1 / 0.22	**Complications** **3-month follow-up** Primary end-point was death or major complication (reoperation, mechanical support, cardiac arrest, coma, stroke, or renal dialysis) at 3 months follow up. The off-pump group had a higher rate of death or major complication 7.0% (77/1104) compared with the on-pump group 5.6% (61/1099) but the difference was not significant ($p = 0.19$). **30-day follow-up** Complications before discharge or up to 30 days. Outcome / Off pump / On pump / p Death / 1.6% (18/1104) / 1.2% (13/1099) / 0.47 Cardiac arrest / 1.8% (20/1104) / 1.1% (12/1099) / 0.21 Renal dialysis / 0.8% (9/1104) / 0.9% (10/1099) / 0.82 Stroke / 1.3% (14/1104) / 0.7% (8/1099) / 0.28 Coma / 0.4% (4/1104) / 0.3% (3/1099) / 1.00 Repeat cardiac surgery / 0.6% (7/1104) / 0.7% (8/1099) / 1.00 Reoperation for bleeding / 2.7% (30/1104) / 2.1% (23/1099) / 0.40 Mechanical support / 1.5% (17/1104) / 0.8% (9/1099) / 0.17 Mediastinitis / 1.0% (11/1104) / 1.3% (14/1099) / 0.55 Tracheostomy / 0.5% (5/1104) / 0.6% (7/1099) / 0.58 **1-year follow-up** 1-year death, or non-fatal MI/requirement for repeat revascularisation between 1 month and 1 year, occurred more frequently in the off-pump group 9.5% (105/1104) than in the on pump group 7.1% (78/1099) ($p = 0.04$). Per-protocol analysis excluding patients who were converted to the other procedure demonstrated no significant difference between the groups in terms of 1-year composite endpoint (p=0.08). Off-pump group 9.4%, on-pump group 7.1%.	**Follow-up issues**: Prospective follow up. 43 patients in the off-pump group and 49 patients in the on-pump group were lost to follow up, withdrew, had poor health or were not followed up for other reason. **Study design issues**: 18 participating centres. All surgeons needed to have performed at least 20 off-pump CABG procedures before participation. Block randomisation by surgeon. Angiograms and neuropsychological tests undertaken blind to treatment group. Significantly more patients in the off-pump group (12.4%) than the on-pump group (3.6%) had their surgery converted to the opposite procedure ($p < 0.001$). Power calculation made for primary end points. Analysis undertaken on intention to treat principle unless stated. **Study population issues**: There were no significant differences between the groups at baseline in terms of clinical or demographic characteristics. Patients enrolled in the study

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial			
Study details	**Key efficacy and safety findings**		**Comments**
Shroyer A L (2009) cont.			had a significantly lower predicted risk of death to 30 days (1.9%) than those who were excluded (2.5%) ($p < 0.001$). **Other issues**: Significantly more patients in the on-pump group (64.0%) than the off-pump group (55.4%) had surgery performed by a resident as the primary surgeon ($p < 0.001$).

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings		Comments
Bridgewater B (2008)[8] Society for Cardiothoracic Surgery in GB and Ireland **National registry** UK Recruitment period: 2004 to 2008 Study population: patients undergoing CABG **n = 208,166 since 1999 (both off-pump and on pump)** Age: off pump 54% >65 years, on pump 55% > 65 years Sex: off pump 20% female, on pump 195 female. Patient selection criteria: Not reported Technique: patients undergoing isolated CABG **Follow-up: not reported** Conflict of interest/source of funding: Supported by medical grants and manufacturers. Report produced by a commercial clinical database company	Number of patients analysed: **n = 208,199 overall.** **Operative characteristics** The rate of off-pump CABG in the UK increased from 9% in 1999 to 19% in 2001, and stabilised to about 17% in 2008. **Survival** Medium-term survival for 2004 to 2008 (n = 86,047) At 1 year follow up survival was 96.5% for off-pump CABG and 96.0% for on-pump CABG. By 5 years, follow-up survival was 88.5% for off-pump CABG and 89.0% for on-pump CABG. (absolute figures not reported)	**Complications** Crude mortality rate (n = 110,001) Overall (for both off-pump and on-pump CABG) % mortality (standard deviation) 2004: Overall 1.9%; Off pump 1.4% (1.1 to 1.9); On pump 2.0% (1.8 to 2.2) 2008: Overall 1.5%; Off pump 0.8% (0.6 to 1.3); On pump 1.6% (1.4 to 1.8) (measurement of significance, absolute figures, and length of follow-up not reported) **In hospital mortality** Regression modelling included demographic and clinical factors at baseline that might influence survival following CABG. Model 1 retained all variables whether statistically significant or not, model 2 used backwards elimination of non-significant variables. Model 1 (n = 69,206) Risk factors for in hospital mortality (2004 to 2008) Factor — Odds ratio (95% CI) On-pump CABG — 1.26 (0.63 to 2.52)* Age — 1.07 (1.04 to 1.10) Emergency procedure — 2.95 (1.34 to 6.52) Salvage procedure — 9.74 (3.89 to 24.38) Previous surgery — 4.09 (2.20 to 7.58) Renal disease — 3.13 (1.94 to 5.06) Extracardiac arteriopathy — 1.68 (1.09 to 2.61) Poor ejection fraction — 2.85 (1.54 to 5.28) Ventilation — 2.09 (1.06 to 4.09) * Not statistically significant Model 2 (n = 78,741) This model excluded off- or on-pump CABG as a factor as it was not significant in model 1. Age and emergency operations (among others) remained significant factors for survival	**Follow-up issues**: Prospective data collection Data completeness (2004 to 2008) ranged from 0.07% missing for patient gender to 6.9% for previous MI. Authors state that data coverage is 100% for all CABG procedures in the last 5 years. **Study design issues**: none **Study population issues**: Off-pump patients were less likely to be undoing non-elective surgery (28% vs 32% for on-pump), and have a fair or poor left ventricular ejection fraction at baseline (28% vs 34%) for on-pump. **Other issues**: The database reported outcomes of patients having CABG in combination with other procedures, but only data from patients having CABG-alone is reported here. Most figures reported here are estimated from graphs in the study report. Authors state that regression models may be subject to bias from decision-making and selection factors that are not included in the database, such as quality of the target vessels. A definitive answer to whether on- or off-pump surgery is safer will only come from randomised clinical trial data.

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings		Comments
Magee M J (2008)[4] PREVENT IV trial subanalysis **Non-randomised controlled study** USA Recruitment period: 2002 to 2003 Study population: patients undergoing CABG n = **3014 (637 off-pump vs 2377 on pump)** Age: 64 years (mean) Sex: 21% female Patient selection criteria: Not reported Technique: Off-pump CABG vs on-pump CABG (techniques not described) the location of target vessels was similar in both groups **Follow-up: 2 years (median)** Conflict of interest/source of funding: one of the authors has a financial relationship with manufacturer	Number of patients analysed: **3,014 (2,400 for angiographic follow up)** ***Graft success*** Graft quality post-procedure (n = number of grafts) Off pump n = 8037 / On pump n = 2072 Good 85.0% / 81.5% Fair 12.9% / 15.9% Poor 2.1% / 2.6% p = 0.001 (absolute figures not reported) Target artery quality post procedure (number of grafts) Off pump n = 8125 / On pump n = 2061 Good 68.1% / 63.8% Fair 22.7% / 26.4% Poor 9.2% / 9.8% p < 0.001(absolute figures not reported) ***Graft efficacy*** Angiographic follow up at 12 to 18 months Off pump n = 402 / On pump n = 1518 / p Graft failure (≥ 75% stenosis): 45.0% (181/402) / 45.9% (697/1518) / 0.75 Occlusion in 1 or more graft: 41.5% (167/402) / 41.7% (633/1518) / 0.92 ***Operative characteristics*** Group median (interquartile range) Off pump n = 681 / On pump n = 1518 / p Length of intensive care sta□□(hours): 25 (21 to 43) / 26 (22 to 48) / 0.006 Length of stay (days): 7 (6 to 10) / 8 (6 to 11) / < 0.001	**Complications** Major adverse outcome (death, stroke, or MI) at 1-year follow-up. Outcome / Off pump / On pump / p Major event: 11.3% (72/637) / 15.4% (367/2377) / 0.012 After adjusting for factors that influence major adverse outcomes (age, sex, smoking status, history of heart failure, history of atrial fibrillation, and number of grafts implanted) on-pump surgery remained a significant predictor of a major adverse outcome at 1-year follow-up (hazard ratio 1.31 [95%] CI 1.01 to 1.69). At 2 years follow-up there was no statistically significant difference between the groups in terms of major adverse events.	**Follow-up issues**: loss to follow-up not reported. **Study design issues**: Although the study was an RCT, it was designed to test a product to prevent vein graft failure, and the decision to perform CABG on-pump or off-pump was not randomised but determined by the surgeon's preference. **Study population issues**: Patients in the off-pump group were significantly older than the on-pump group (p = 0.013), and had more grafts implanted (p < 0.001). Also fewer patients in the off-pump group were having urgent, emergency, or salvage surgery (p < 0.001). **Other issues**: The number of patients which received the active intervention in each group is not reported. However, analysis showed that it had no significant effect over placebo. The method of vein graft harvesting (open vs endoscopic) was at the discretion of the operating surgeon. Significantly more patients in the on-pump group had vein grafts harvested in by the endoscopic technique (p < 0.001).

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings	Comments
Mishra M (2006)[5] **Non-randomised controlled study** India Recruitment period: 1995 to 2004. Study population: patients undergoing CABG with aortic atheromatous disease (as assessed by transoesophageal echocardiography). Carotid artery disease present in 7.7% of patients n = **6000 (3000 off-pump vs 3000 on-pump)** Age: 59 years (mean) Sex: 13% female. Patient selection criteria: Not reported Technique: In both groups technique of CABG was individualised for each patient to avoid atheroembolism. Off-pump CABG (combined with coronary angioplasty or laser revascularisation in some patients vs on-pump CABG) **Follow-up: not reported (to discharge)** Conflict of interest/source of funding: not reported	Number of patients analysed: **6000 (3000 off pump vs 3000 on pump)** ***Operative characteristics*** Group mean (standard deviation) Off pump n = 3000 / On pump n = 3000 / p Number of grafts: 3.05 ± 0.82 / 3.24 ± 0.84 / < 0.001 Length of intensive care stay (hours): 20 ± 7 / 32 ± 8 / < 0.001 Length of stay (days): 6 ± 2 / 8 ± 3 / < 0.001 **Complications** Rate of occurrence of intraoperative and postoperative events Off pump n = 3000 / On pump n = 3000 / p Hospital mortality: 1.4% (42/3000) / 3.0% (90/3000) / < 0.001 Reoperation for bleeding: 2.1% (64/3000) / 4.3% (129/3000) / < 0.001 Deep wound infection: 0.6% (18/3000) / 1.3% (38/3000) / 0.01 Renal failure: 1.3% (39/3000) / 2.2% (66/3000) / 0.01 Ventilation >24 hours: 4.4% (132/3000) / 7.8% (234/3000) / < 0.001 Gastrointestinal bleeding: 1.0% (29/3000) / 1.1% (33/3000) / 0.70 Stroke: 0.5% (15/3000) / 1.0% (29/3000) / 0.05 Multivariate analysis indicated that history of stroke or cerebrovascular disease (p = 0.016), left ventricular ejection fraction ≤ 0.30 (p = 0.049), heart failure (p < 0.001), acute MI (p < 0.008), age ≥ 70 years (p < 0.001), male sex (p = 0.034), and diabetes (p = 0.076) were independent predictors of hospital mortality.	**Follow-up issues**: retrospective study. 6000 patients matched from 6991 with aortic atheromatous disease undergoing CABG. **Study design issues**: propensity matched pairs analysis, based on age, acute MI, heart failure, hypertension, and diabetes mellitus. Off-pump CABG was undertaken more often in the later years of the study. **Study population issues**: The demographic and clinical characteristics of the two groups at baseline was well-matched with a propensity score difference of 0.005.

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings		Comments
Synnergren M J (2008)[6] **Non-randomised controlled study** Sweden Recruitment period: 1995 to 2004. Study population: n = **9408 (947 off pump vs 8461 on pump)** Age: years (mean) Sex: % female. Patient selection criteria: Not reported Technique: Off-pump vs on-pump CABG (techniques not described) at the preference of the surgeon. **Follow-up: 5 years mean (significantly longer in the on pump group p = 0.002)** Conflict of interest/source of funding: not reported	Number of patients analysed: **9408 (947 off pump vs 8461 on pump)** ***Mortality*** The primary end point was all-cause mortality. The overall mortality was significantly lower in the off-pump group (9.4%) than in the on-pump group (13.3%) (p<0.001) (absolute figures not reported). The use of on-pump or off-pump technique was not significantly associated with hazard ratio for death when incomplete revascularisation was included as a variable Hazard ratio 1.08 (95% CI 0.82 to 1.40) (p = 0.57). ***Operative characteristics*** Group mean (standard deviation) Off pump n = 957 / On pump n = 8461 / p Complete revascularisation: 67.1% (642/957) / 82.8% (7010/8461) / < 0.001 Incomplete revascularisation, 1 segment: 24.1% (231/957) / 16.6% (1401/8461) / < 0.001 Incomplete revascularisation, 2 segments: 7.7% (74/957) / 0.6% (50/8461) / < 0.001	**Complications** 'Early mortality' (not otherwise defined) was not significantly different between the off-pump group 1.1% and the on-pump group 1.6% (p = 0.28) (absolute figures not reported).	**Follow-up issues**: Retrospective study. Only 9,408/11,647 of patients with complete data available are included in the analysis. No significant difference in the proportion of patients available between the groups. Outcome was assessed using a national population register. **Study design issues**: Stepwise multiple regression analysis to account for factors that influence hazard ratio. **Study population issues**: Factors that favoured selection for off-pump technique included: well-sized noncalcified arteries with epicardial location, extensive aortic calcifications, previous stroke, or multiple comorbidity. Patients in the off-pump group were older, predominantly female, undergoing a planned operation, and had a higher left ventricular ejection fraction, less had hypertension, or a previous MI, all (p < 0.001). More patients in the off-pump group had one vessel disease, proximal left anterior descending artery stenosis, (p < 0.001). **Other issues**: None

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings		Comments
Agostini M (2009)[9] **Case series** Italy Recruitment period: 2000 to 2005 Study population: patients requiring CABG. 26% (312/1183) of patients selected for off pump CABG n = **312** Age: 69 years (mean) Sex: 82 % female. Patient selection criteria: Not reported Technique: Off-pump CABG with artery stabilisation with a disposable suction device **Follow-up: 42 months (mean)** Conflict of interest/source of funding: not reported	Number of patients analysed: **312** ***Revascularisation*** Complete revascularisation was achieved in 66.3% (207/312) of patients. Higher age ($p < 0.0001$), ejection fraction <30% ($p = 0.040$) and obesity ($p = 0.048$) were predictors of incomplete revascularisation (bivariate analysis); however, number of diseased vessels ($p = 0.06$) was not significantly associated with outcome. ***Operative characteristics*** The conversion rate to on-pump CABG was 3.8% (12/312)	**Complications** Outcome / Rate Death up to 30 days: 1.3% (4/312) Cardiac death: 0.6% (2/312) Stroke: 0.6% (2/312) MI: 4.5% (14/312) Non q-wave MI: 3.5% (11/312) There was no significant difference in the rate of complications between patients who achieved complete revascularisation and those with incomplete revascularisation.	**Follow-up issues**: 10.5% (33/312) of patients underwent follow-up angiography. **Study design issues**: Off-pump CABG technique evolved during the recruitment period. Study focused on prognostic factors for complete revascularisation. **Study population issues**: Patient selection criteria for off-pump rather than on-pump CABG not reported. **Other issues**: None.

Abbreviations used: CABG, coronary artery bypass graft; CI, confidence interval; MI, myocardial infarction; RCT, randomised controlled trial

Study details	Key efficacy and safety findings	Comments
Ueno T (2006)[7] **Case report** Japan Recruitment period: Not reported. Study population: n = **1** Age: 72 years (mean) Sex: 0% female Patient selection criteria: Not reported Technique: Off-pump CABG **Follow-up: 13 days** Conflict of interest/source of funding: not reported	**Post-procedural ST elevation MI and cardiogenic shock.** About 10 minutes after extubation following off-pump CABG, the patient suddenly went into shock, in association with ST elevation, and ventricular fibrillation on electrocardiogram. Coronary spasm of the right coronary artery was suspected and transcatheter intraluminal injection of several vasodilators failed to relieve the spasm. The patient remained in profound cardiogenic shock due to broad acute MI and died of multiple organ failure.	**Follow-up issues**: not clear how many patients were treated at the institution (the denominator) **Study design issues**: None **Study population issues**: None **Other issues**: Surgeon's prior experience of this procedure is not reported. Coronary spasm might be a complication of on-pump surgery too.

Efficacy

Survival

A UK national registry of more than 200,000 patients treated since 1999 (with approximately 17% of procedures being undertaken with off-pump CABG in 2008) reported that 1-year survival for patients treated in the period 2004 to 2008 was 97% for off-pump CABG and 96.0% for on-pump CABG. By 5 years follow-up for patients who had reached that time point, survival was 89% for off-pump CABG and 89% for on-pump CABG (measurement of significance and absolute figures were not reported) [8].

Graft patency

A randomised controlled trial of 2203 patients reported that on angiographic assessment significantly fewer grafts remained patent at 12-month follow-up following off-pump CABG 83% (1650/1998) than following on-pump CABG 88% (1839/2095) ($p < 0.001$)[3].

A non-randomised controlled study of 3014 patients reported that graft failure (≥ 75% stenosis) occurred in 45% (181/402) of patients in the off-pump group and in 46% (697/1518) of patients in the on-pump group at angiographic follow-up between 12 and 18 months ($p = 0.75$)[4]. In the same study, occlusion of 1 or more vein grafts occurred in 42% (167/402) and 42% (633/1518) of patients respectively ($p = 0.92$).

Number of grafts

A randomised controlled trial of 2203 patients reported that significantly more patients in the off-pump group (18%) had fewer grafts inserted during the procedure than planned preoperatively than patients in the on-pump group (11%) ($p < 0.001$) (absolute figures not reported)[3].

Safety

Studies report several outcomes that can be interpreted as either efficacy or safety outcomes depending on the length of follow-up (post-operative period or not). For convenience, such outcomes are reported here in the ‘safety’ section, although it is acknowledged that some outcomes such as mortality or revascularisation if they occur beyond 30-days after the operation usually indicate lack of efficacy, and are not as such ‘safety’ outcomes.

Composite endpoints

A randomised controlled trial of 2203 patients reported that death, MI, or revascularisation between 1-month and 1-year follow-up occurred more frequently in the off-pump group 10% (105/1104) than in the on-pump group 7% (78/1099) ($p = 0.04$)[3]. A non-randomised controlled study of 3014 patients

reported that major adverse events (death, stroke, or MI) occurred significantly less frequently in the off-pump group 11% (72/637) than in the on-pump group 15% (367/2377) at 1-year follow-up ($p = 0.012$)[4].

Mortality

A meta-analysis of randomised controlled trials totalling 5537 patients reported that there was no statistically significant difference between off-pump and on-pump CABG in pooled mortality rate (relative risk 0.98 [95%] CI 0.66 to 1.44) (length of follow-up not reported)[1]. A meta-analysis of 297,000 patients reported that 30-day mortality was significantly lower following off-pump rather than on-pump CABG in non-randomised studies (pooled odds ratio 0.72 [95%] CI 0.66 to 0.78) ($p < 0.00001$)[2]. A randomised controlled trial of 2203 patients reported no statistically significant difference in death to 30 days follow-up between the off-pump group 2% (18/1104) and the on-pump group 1% (13/1099) ($p = 0.47$)[3].

A UK national registry of over 200,000 patients treated since 1999 (with approximately 17% of procedures being undertaken with off-pump CABG in 2008) reported that overall mortality for all patients undergoing CABG decreased from 1.9% in 2004 to 1.5% in 2008. Mortality for patients undergoing off-pump CABG decreased from 1.4% in 2004 to 0.8% in 2008 (measurement of significance, absolute figures, and length of follow up not reported)[8].

Stroke

A meta-analysis of 297,000 patients reported that stroke occurred significantly less frequently following off-pump CABG than on-pump CABG (pooled odds ratio 0.62 [95%] CI 0.55 to 0.69) in non-randomised studies ($p < 0.00001$) (length of follow-up not reported)[2]. A non-randomised controlled study of 6000 patients reported that stroke occurred significantly less frequently in the off-pump group (< 1%, 15/3000) than in the on-pump group (1%, 29/3000) at follow-up to discharge ($p = 0.05$)[5].

Revascularisation

A meta-analysis of randomised controlled trials totalling 5537 patients reported that there was no statistically significant difference between off-pump and on-pump CABG in pooled rate of need for revascularisation (relative risk 1.35 [95%] CI 0.83 to 2.18) (length of follow-up not reported)[2].

A meta-analysis of 297,000 patients reported that there was no statistically significant difference in the rate of need for revascularisation between off-pump and on-pump CABG in non-randomised studies (pooled odds ratio 1.35 [95%] CI 0.76 to 2.39) ($p = 0.31$) (length of follow-up not reported)[1].

Other adverse events

One case report described coronary spasm of the right coronary artery with profound cardiogenic shock and death due to multiple organ failure at 13-day follow-up[7].

Validity and generalisability of the studies

- All comparative studies used on-pump CABG as a comparator.
- Few angiographically assessed efficacy outcomes are reported in the studies.
- Studies include a mix of patients in terms of risk profile. In non-randomised trials, patient-selection for off-pump surgery may have prioritised patients with comorbidities.

Existing assessments of this procedure

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S): Off-pump coronary artery bypass surgery with the aid of the Octopus Tissue Stabilizer (OTS) (2001 update)

Conclusion

The ASERNIP-S Review Group concluded that the updated evidence base for OPCAB/OTS was still inadequate for establishing its safety and efficacy. The original ASERNIP-S safety and efficacy classification of '2', with a recommendation for an audit of OPCAB/OTS, was upheld.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- CURRENT GUIDANCE Off-pump coronary artery bypass (OPCAB). NICE interventional procedures guidance 35 (2004). Available from www.nice.org.uk/guidance/IP35

Technology appraisals

- TA 152 Drug-eluting stents for the treatment of coronary artery disease NICE technology appraisal152 (2008). Available from www.nice.org.uk/guidance/TA152

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr S Kendall, Mr T Pillay, and Mr M Pullan, (Society of Cardiothoracic Surgery of Great Britain and Ireland)

- All three Specialist Advisers classifies this procedure as established and no longer new.
- The main comparator is on-pump CABG.
- The key efficacy outcomes for this procedure include mortality, requirement for additional revascularisation, symptoms, and length of stay.
- Adverse events following this procedure have included aortic dissection, perioprtative myocardial infarction, haemodynamic compromise, emergency conversion to on-pump CABG, incomplete grafting, and early graft occlusion.
- Additional theoretical adverse events relating to this procedure as similar to those with on-pump CABG including death, stroke, infection, bleeding, and renal dysfunction. Also, inaccurate suturing may lead to graft failure.
- One adviser commented that there is a large variation in techniques for off-pump CABG.
- Mentored teaching is available to trainees and consultants.
- One adviser noted that there is no higher risk than with conventional bypass surgery when carried out by an experienced surgeon.
- The CRIPS randomised controlled trial is and MRC funded randomised controlled trial comparing off-pump and on-pump CABG in high risk patients (those 70+ or men with < 50% left ventricular ejection fraction and with Euroscore of ≥ 5). It is being coordinated at the Bristol Heart Institute and

plans to recruit 5000 patients in 40 UK and worldwide centres, and will record outcomes to 1 year follow-up.

- One adviser commented that the benefit of off-pump CABG is more apparent in high risk groups. Comparing to the standard technique in low risk groups shows marginal benefit.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 30 questionnaires to 1 trust for distribution to patients who had the procedure (or their carers). NICE received 16 completed questionnaires.

The Patient Commentators' views on the procedure were consistent with the published evidence and the opinions of the Specialist Advisers.

Issues for consideration by IPAC

- No equalities issues were raised during scoping.
- Considerable additional data are available in appendix A.
- Review of guidance was elicited due to safety concerns.
- Much of the randomised controlled trials and non-randomised controlled studies are summaries in the two meta-analyses included in table 2. Other more recent studies are also included in table 2.
- The committee may wish to consider requesting further synthesis of the available data to date particularly regarding the key safety outcomes, or long-term patency outcomes from the IP review body.

References

1 Møller CH, Penninga L, Wetterslev J et al. (2008) Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. Cochrane Database of Systematic Reviews: Protocols issue 3.

2 Wijeysundera DN, Beattie WS, Djaiani G et al. (2005) Off-pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. Journal of the American College of Cardiology 46(5): 872–82.

3 Shroyer AL, Grover FL, Hattler B et al. (2009) On-pump versus off-pump coronary-artery bypass surgery. The New England Journal of Medicine 361:1827–37.

4 Magee MJ, Alexander JH, Hafley G et al. (2008) Coronary artery bypass graft failure after on-pump and off-pump coronary artery bypass: findings from PREVENT IV. The Annals of thoracic surgery 85: 494–9.

5 Mishra M, Malhotra R, Karlekar A et al. (2006) Propensity case-matched analysis of off-pump versus on-pump coronary artery bypass grafting in patients with atheromatous aorta. Annals of Thoracic Surgery 82: 608–14.

6 Synnergren MJ, Ekroth R, Oden A et al. (2008) Incomplete revascularization reduces survival benefit of coronary artery bypass grafting: role of off-pump surgery. Journal of Thoracic and Cardiovascular Surgery 136: 29–36.

7 Ueno T, Ikeda K, Nakashima A (2006) Vasodilator resistant lethal spasm after uncomplicated off-pump coronary surgery. Asian Cardiovascular and Thoracic Annals 14: 158–60.

8 Bridgewater B, Keogh B, Kinsman R, et al. (2008) The Society for Cardiothoracic Surgery in Great Britain and Ireland. Sixth National Adult Cardiac Surgical Database Report. Demonstrating quality.

9 Agostini M, Fino C, Torchio P et al. (2009) Impact of incomplete revascularization following OPCAB surgery. Journal of Cardiac Surgery 24: 650–6.

Appendix A: Additional papers on off-pump coronary artery bypass grafting

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Alhabash O, Tirouvanziam A, Roussel JC et al. (2003) Early and 1 year angiographic evaluation of graft patency in off-pump coronary bypass surgery via sternotomy. Interactive Cardiovascular and Thoracic Surgery 2 (2) 149–153.	n = 87 Follow up = 1 year	Most of the stenosis detected at the early coronary angiography could decrease or disappear, especially in arterial grafts.	Larger studies are included in table 2
Allen GS (2008) Intraoperative temperature control using the Thermogard system during off-pump coronary artery bypass grafting. Annals of Thoracic Surgery 87 (1) 284–288.	n = 38 Follow up = not reported	Endovascular warming is safe, simple to use, and obviates the need for uncomfortably warm operating room temperatures. The Thermogard system compared favorably with conventional methods for warming during off-pump CAB.	Larger studies are included in table 2
Ankeney JL and Goldstein DJ (2007) Off-pump bypass of the left anterior descending coronary artery: 23- to 34-year follow-up. Journal of Thoracic & Cardiovascular Surgery 133 (6) 1499–1503.	n = 241 Follow up = 23 to 34 years	Off-pump bypass of the left anterior descending coronary artery with an internal thoracic artery can be done on a beating heart safely and results in median survival of patients for more than 23 years.	Larger studies are included in table 2
Arora D, Juneja R, Pendarkar D, et al. (2007) Off-pump coronary artery bypass grafting in a polycythaemic patient--case report and review of literature. Annals of Cardiac Anaesthesia 10 (1) 54–57.	n = 1 Follow up = 6 months	A multimodal approach involving various specialities to confirm the diagnosis and control of the disease process prior to surgery and in the perioperative period is recommended.	Larger studies are included in table 2

Ascione R, Reeves BC, Pano M et al. (2004) Trainees operating on high-risk patients without cardiopulmonary bypass: a high-risk strategy? Annals of Thoracic Surgery 78 (1) 26–33.	n = 686 Follow up = 1.7 years	Off-pump coronary artery bypass grafting surgery in high-risk patients can be safely performed by trainees.	Larger studies are included in table 2
Baba T, Goto T, Maekawa K, et al. (2007) Early neuropsychological dysfunction in elderly high-risk patients after on-pump and off-pump coronary bypass surgery. Journal of Anesthesia 21 (4) 452–458.	n = 218 Follow up = not reported	Off-pump CABG reduced postoperative NP dysfunction in elderly patients with severe systemic atherosclerosis compared with on-pump CABG.	Larger studies are included in table 2
Mannam G, Sajja LR, Dandu SB et al. (2008) Off-pump coronary revascularization for left main coronary artery stenosis. Asian Cardiovascular & Thoracic Annals 16 (6) 473–478.	n = 379 Follow up = not reported	There were 2 operative deaths in the on-pump group and 1 in the off-pump group. The off-pump procedure is safe and effective in patients with left main coronary artery disease.	Larger studies are included in table 2
Beauford RB, Saunders CR, Lunceford TA et al. (2005) Multivessel off-pump revascularization in patients with significant left main coronary artery stenosis: early and midterm outcome analysis. Journal of Cardiac Surgery 20 (2) 112–118.	n = 654 Follow up = to 3 months	Multivessel off-pump revascularisation in patients with severe left main disease is a safe and effective alternative to conventional bypass grafting and conveys a survival benefit.	Larger studies are included in table 2
Behny LP (2006) Off-pump coronary artery baypass grafting: A case report. AANA Journal 74 (1) 39–44.	n = 1 Follow up = 4 days	A case report of a 72-year-old female who underwent off-pump CAB is outlined.	Larger studies are included in table 2
Berdat PA, Muller K, Schmidli J, et al. (2004)Total arterial off-pump versus on-pump coronary revascularization:	n = 149 Follow up = not reported	Arterial off-pump CAB patients have less extensive coronary artery disease, but more severe symptoms. Early outcome is similar concerning	Larger studies are included in table 2

comparison of early outcome. Journal of Cardiac Surgery 19 (6) 489–494.		mortality, arrhythmias, cerebro-vascular accidents, renal failure, or intensive care unit and hospital stay.	
Bergsland J, Lingaas P S, Skulstad H, et al. (2009) Intracoronary shunt prevents ischemia in off-pump coronary artery bypass surgery Annals of Thoracic Surgery 87 (1) 54–60.	n = 56 Follow up = 3 months	Intracoronary shunt prevents ischemia during grafting of the left anterior descending coronary artery and provides satisfactory immediate and short-term graft patency.	Larger studies are included in table 2
Bonatti J, Nagele G, Hangler H et al. (2002) Extraanatomical coronary artery bypass grafts on the beating heart for management of the severely atherosclerotic ascending aorta. Heart Surgery Forum 5 Suppl-81.	n = 22 Follow up = 8 months	Performance of beating heart extraanatomical coronary artery bypass grafts for management of a heavily diseased ascending aorta can result in a very low stroke rate despite a considerable stroke risk.	Larger studies are included in table 2
Bolton JW (2005) Same day discharge following multivessel off-pump coronary artery bypass via sternotomy. Annals of Thoracic Surgery 79 (1) 345–346.	n = 1 Follow up = 14 days	An aggressive perioperative regimen can result in same-day discharge following multivessel off-pump CAB.	Larger studies are included in table 2
Bossert T, Bittne H , Gummert JF et al. (2006) Coronary artery spasm of the native right coronary artery during off-pump coronary surgery of the left coronary artery system. Clinical Research in Cardiology 95 (2): 115–118.	n = 1 Follow up = 10 days	The immediate postoperatively performed coronary angiography demonstrated patent anastomoses and two areas of significant spasticity within the course of the right coronary artery.	Larger studies are included in table 2
Carr CS, Rayner A, Ponte J et al. (2005) Off-pump coronary artery bypass grafting in a heparin-induced thrombocytopenia type II patient using hirudin. Annals of Thoracic Surgery 79 (2) 696–698.	n = 1 Follow up = 1 day	The study presents a case in which off-pump CAB grafting was performed in an Heparin-induced thrombocytopenia patient in whom the lower doses of hirudin could safely be monitored with easily available tests.	Larger studies are included in table 2

Carr C and Desai J (2004) OPCAB surgery in a cirrhotic hepatocellular carcinoma patient awaiting liver transplant. Annals of Thoracic Surgery 78 (4) 1460–1462.	n = 1 Follow up = 2 months	We present the strategy used in a patient with multifocal hepatocellular carcinoma and cirrhosis who underwent coronary artery bypass grafts for unstable angina, in order to allow him to undergo liver transplantation at a future date.	Larger studies are included in table 2
Carrier M, Robitaille D, Perrault LP et al. (2003) Heparin versus danaparoid in off-pump coronary bypass grafting: Results of a prospective randomized clinical trial. Journal of Thoracic and Cardiovascular Surgery 125 (2) 325–329.	n = 71 Follow up = not reported	Although off-pump CAB grafting with danaparoid versus heparin increases the number of patients exposed to homologous blood transfusion off-pump CAB grafting with danaparoid is a valuable alternative to heparin in patients with thrombocytopenia requiring surgical intervention.	Larger studies are included in table 2
Casselman FP, Meco M, Dom H et al. (20040 Multivessel distal sutureless off-pump coronary artery bypass grafting procedure using magnetic connectors. Annals of Thoracic Surgery 78 (2) e38–e40.	n = 2 Follow up = 1 week	We recently performed two off-pump CAB procedures that were distally completely sutureless.	Larger studies are included in table 2
Christenson JT, Licker M and Kalangos A (2003) The role of intra-aortic counterpulsation in high-risk OPCAB surgery: A prospective randomized study. Journal of Cardiac Surgery 18 (4) 286–294	n = 30 Follow up = not reported	Pre- and perioperative intra-aortic balloon counterpulsation therapy offers efficient hemodynamic support during high-risk off-pump CAB surgery, lowers the risk of hemodynamic instability, is safe and shortens both ICU and hospital length of stay significantly.	Larger studies are included in table 2
Danzmayr M, Riha M, Nagele G et al. (2003) Off-pump coronary artery bypass grafting - Perioperative results and 1-year follow-up. European Surgery - Acta Chirurgica Austriaca 35 (2) 107–110.	n = 149 Follow up = 1 year	Off-pump CAB can achieve perioperative results that are better than those predicted by common risk scores.	Larger studies are included in table 2

Darwazah AK, Sham'a, RA, Isleem I et al. (2009) Off-pump coronary artery bypass for emergency myocardial revascularization. Asian Cardiovascular & Thoracic Annals 17 (2) 133–138.	n = 79 Follow up = 15 to 82 months	Patients treated on an emergency basis should have an off-pump revascularisation procedure.	Larger studies are included in table 2
Demaria RG, Fortier S, Carrier M et al. (2001) Early multifocal stenosis after coronary artery snaring during off-pump coronary artery bypass in a patient with diabetes. Journal of Thoracic and Cardiovascular Surgery 122 (5): 1044–1045.	n = 1 Follow up = 16 months	Occlusive snaring of calcified coronary arteries in diabetic patients during off-pump CABG should be done with caution.	Larger studies are included in table 2
Detter C, Reichenspurner H, Boehm DH et al. (2002) Minimally invasive direct coronary artery bypass grafting (MIDCAB) and off-pump coronary artery bypass grafting (OPCAB): Two techniques for beating heart surgery. Heart Surgery Forum 5 (2) 157–162.	n = 340 Follow up = not reported	Coronary bypass surgery without the use of bypass is feasible and safe, and offers good early results.	Larger studies are included in table 2
Di Giammarco G, Pano M, Giancane M et al. (2006) Off-pump revascularization of chronically occluded left anterior descending artery through left anterior small thoracotomy: early and late angiographic and clinical follow-up.[see comment]. Annals of Thoracic Surgery 82 (4) 1446–1450.	n = 143 Follow up = 8 years	In our experience, left anterior small thoracotomy operation can be considered a suitable choice for treatment of left anterior descending artery chronic occlusion.	Larger studies are included in table 2
Djaiani G, Fedorko L, Cusimano RJ et al. (2006) Off-pump coronary bypass surgery: risk of ischemic brain lesions in patients	n = 26 Follow up = not reported	Patient stratification based upon aortic atheroma burden should be addressed in future trials designed to tailor treatment strategies to improve short-	Larger studies are included in table 2

with atheromatous thoracic aorta. Canadian Journal of Anaesthesia 53 (8) 795–801.		and long-term neurological outcomes in patients undergoing cardiac surgery.	
Drenth DJ, Veeger NJ, GM, Middel B. et al. (2004) Comparison of late (four years) functional health status between percutaneous transluminal angioplasty intervention and off-pump left internal mammary artery bypass grafting for isolated high-grade narrowing of the proximal left anterior descending coronary artery. American Journal of Cardiology 94 (11) 1414–1417.	n = 102 Follow up = 4 years	Although the occurrence of angina (p = 0.036) and major adverse cardiac and cerebrovascular events (p = 0.02) was significantly higher 4 years after angioplasty, functional health status did not differ between treatments and was comparable to a healthy reference population.	Larger studies are included in table 2
Durand M, Chavanon O, Tessier Y et al. (2006) Right ventricular function after coronary surgery with or without bypass. Journal of Cardiac Surgery 21 (1) 11–16.	n = 29 Follow up = not reported	In patients with severe right coronary stenosis, off-pump cardiac surgery seemed to provide better right ventricular protection.	Larger studies are included in table 2
Ennker IC, Pietrowski D, and Ennker J (2006) Off-pump myocardial revascularisation in an octogenarian patient with dextrocardia and situs inversus. Cardiovascular Journal of Southern Africa 17 (5) 257–258.	n = 1 Follow up = 16 days	An 82-year-old woman with dextrocardia and situs inversus totalis underwent successful off-pump CAB grafting using internal mammary arteries.	Larger studies are included in table 2
Fukushima S, Kobayashi J, Tagusari O et al. (2004) Rationale of off-pump coronary artery bypass grafting for left main trunk disease. Japanese Journal of Thoracic and Cardiovascular Surgery 52 (12) 560–566.	n = 257 Follow up = not reported	Off-pump CAB allows a safe and effective treatment of left main trunk disease.	Larger studies are included in table 2
Gal J, Grattan A, Kertai,	n = 44	The trend toward improved	Larger studies are

MD et al. (2007) Coronary revascularization in transition from on-pump to off-pump: the effect of the off-pump coronary artery bypass on medium-term outcome. Journal of Cardiovascular Surgery 48 (1) 67–72.	Follow up = 12 months	medium-term outcome variables among patients treated with off-pump CAB may have owed to the reduced cardiac ischemic injury associated with off-pump CAB compared with on-pump CABG.	included in table 2
Grossi EA, Bizekis CS, Sharony R et al. (2003) Routine intraoperative transesophageal echocardiography identifies patients with atheromatous aortas: impact on "off-pump" coronary artery bypass and perioperative stroke. Journal of the American Society of Echocardiography 16 (7) 751–755.	n = 913 Follow up = not reported	Routine intraoperative transesophageal echocardiography identifies patients with severe atheromatous aortic disease. In these patients, off-pump CAB technique is associated with a lower risk of death, stroke, and all complications.	Larger studies are included in table 2
Gurbuz AT, Hecht ML, and Arslan AH (2007) Intraoperative transesophageal echocardiography modifies strategy in off-pump coronary artery bypass grafting. Annals of Thoracic Surgery 83 (3) 1035–1040.	n = 744 Follow up = to discharge	Intraoperative transesophageal echocardiography is a valuable adjunct and can result in a major change of surgical strategy in a significant number of patients when used routinely for off-pump CAB. It may also improve surgical outcome and add to the off-pump CAB benefits.	Larger studies are included in table 2
Gurbuz AT, Zia AA, Cui H et al. (2004) Predictors of mid-term symptom recurrence, adverse cardiac events and mortality in 591 unselected off-pump coronary artery bypass graft patients. Journal of Cardiac Surgery 21 (1) 28–34.	n = 591 Follow up = 39 months	Off-pump CAB grafting can be performed with low-symptom recurrence, adverse cardiac events, and mortality rates. Modification of intra- and postoperative management strategies may improve outcomes.	Larger studies are included in table 2
Hamman BL and White CH (2004) A novel device for clampless proximal	n = 76 Follow up = not	We found the device to be a useful adjunct for minimally invasive CAB	Larger studies are included in table 2

anastomosis in OPCAB surgery: The IPAD. Heart Surgery Forum 7 (5) 272–273.	reported	graft surgery.	
Hashimoto M, Aoki M, Okawa Y et al. (2006) Massive pulmonary embolism after off-pump coronary artery bypass surgery. Japanese Journal of Thoracic & Cardiovascular Surgery 54 (11) 486–489.	n = 1 Follow up = 3 days	A repeat echocardiogram revealed enlargement of the right ventricle. Multislice computed tomography showed a massive embolus in the pulmonary artery. Surgical embolectomy was performed, and the patient's postoperative course was easy.	Larger studies are included in table 2
Hirose, H. (2004) Off-Pump Coronary Artery Bypass Grafting for Patients with Left Main Disease. Cardiology 101 (4) 194–198.	n = 147 Follow up = 2.1 years	Our observations support off-pump CABG as a surgical option with a favorable outcome for patients with left main disease.	Larger studies are included in table 2
Horimoto S, Horimoto, H, Sawada Y et al. (2005) Off-pump coronary artery bypass in a patient with the antiphospholipid syndrome. Journal of Cardiovascular Surgery 46 (1) 81–83.	n = 1 Follow up = 3 years	The procedure was successful, and the postoperative course for 3 years has been satisfactory without any cardiovascular complaints.	Larger studies are included in table 2
Ibrahim K, Vitale N, Kirkeby-Garstad I et al. (2008) Narrowing effect of off-pump CABG on the LIMA-LAD anastomosis: Epicardial ultrasound assessment. Scandinavian Cardiovascular Journal 42 (2) 105–109.	n = 50 Follow up = not reported	Off-pump CABG may cause a narrowing of the coronaries, especially at the anastomotic heel. The anastomotic technique at the heel may have to be modified to improve its patency.	Larger studies are included in table 2
Imamaki M, Matsuura K, Sakurai M et al. (2009) Evaluation of early and midterm results of offpump coronary artery bypass in patients with left main disease. Journal of Cardiac Surgery 24 (2) 162–166.	n = 206 Follow up = not reported	Patients with left main coronary artery stenosis can undergo off-pump CAB safely and the midterm results are good.	Larger studies are included in table 2
Inoue Y, Lim RC, and Nand P	n = 1	The combination of off-pump CABG and	Larger studies are included in table 2

(2004) Coronary artery bypass grafting in an immune thrombocytopenic purpura patient using off-pump techniques. Annals of Thoracic Surgery 77 (5) 1819–1821.	Follow up = 5 days	preoperative IgG therapy appears to be an ideal strategy for idiopathic thrombocytopenic purpura patients requiring coronary revascularisation.	
Ito K, Kawachi H, Nishiyama K et al. (2003) Off-pump coronary artery bypass grafting in a patient with chronic myelomonocytic leukemia. Japanese Heart Journal 44 (3) 435–439.	n = 1 Follow up = 6 months	Off-pump coronary artery bypass grafting is safe and useful for high risk patients, such as those with leukemia.	Larger studies are included in table 2
Izutani H, Yoshitatsu, M, Kawamoto J, et al. (2005) A case of ostial stenosis with the PAS-Port proximal anastomosis system in off-pump coronary artery bypass grafting. Interactive Cardiovascular and Thoracic Surgery 4 (4): 341–343.	n = 13 Follow up = not reported	1 patient developed severe ostial and proximal graft stenosis identified at 4 months postoperative angiogram.	Larger studies are included in table 2
Jo W-M, Na C-Y, Baek, M-J et al. (2004) Application of cabrol technique to off-pump coronary artery bypass grafting using radial artery. Annals of Thoracic Surgery 78 (3) 1081–1082.	n = 1 Follow up = 4 days	In selected patients, we suggest that this technique allows the effective use of graft length and can reduce a number of ascending aortic manipulations.	Larger studies are included in table 2
Kakinohana M, Abe M, Kamizato K et al. (2006) Right coronary artery spasms triggered by mechanical compression during off-pump coronary artery bypass grafting surgery. Journal of Anesthesia 20 (1): 30–32.	n = 1 Follow up = 18 hours	From our experience, we should be aware that mechanical compression may trigger an exaggerated vasomotor response, leading to severe coronary artery spasms.	Larger studies are included in table 2
Kazaz H, Ustunsoy H, Celkan M A et al. (2006) Midterm results of off-pump coronary artery bypass surgery in 136	n = 136 Follow up = 2 years	Off-pump CAB graft is efficient procedure with lower index of mortality, morbidity, ICU stay, hospital stay, good wound	Larger studies are included in table 2

patients: an angiographic control study. Journal of Cardiac Surgery 21 (1) 6–10.		healing, early socialization, and results in lower costs.	
Khan N E, De Souza A, Mister R et al. (2004) A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgeryNew England Journal of Medicine 350 (1) 21–28.	n = 104 Follow up = 3 months	Off-pump coronary surgery was as safe as on-pump surgery and caused less myocardial damage. However, the graft-patency rate was lower at three months in the off-pump group than in the on-pump group, and this difference has implications with respect to the long-term outcome.	Larger studies are included in table 2
Kim K B, Cho KR and Jeong DS (2008) Midterm angiographic follow-up after off-pump coronary artery bypass: serial comparison using early, 1-year, and 5-year postoperative angiograms. Journal of Thoracic & Cardiovascular Surgery 135 (2) 300-307.	n = 240 Follow up = 5 years minumum	Midterm angiographic follow-up demonstrated acceptable patency rates of grafts after off-pump coronary artery bypass surgery.	Larger studies are included in table 2
Kon ZN, Brown EN, Tran R et al. (2008) Simultaneous hybrid coronary revascularization reduces postoperative morbidity compared with results from conventional off-pump coronary artery bypass. Journal of Thoracic & Cardiovascular Surgery 135 (2) 367–375.	n = 45 Follow up = 1 year	Perhaps because of reduced myocardial injury, inflammation, and activation of coagulation, patients undergoing the hybrid procedure had better perioperative outcomes and satisfaction, with excellent patency at 1 year's follow-up.	Larger studies are included in table 2
Lawton J S, Deshpande S P, Zanaboni P B et al. (2005) Spontaneous atrioventricular groove disruption during off-pump coronary artery bypass grafting. Annals of Thoracic Surgery 79 (1): 339–341.	n = 1 Follow up = 15 days	Significant distortion of the mitral annulus and elevation of pulmonary artery pressures in the beating heart likely contributed to the spontaneous tear.	Larger studies are included in table 2
Lev-Ran O, Braunstein R, Sharony R, et al.	n = 700	The results are reproducible and	Larger studies are included in table 2

(2005) No-touch aorta off-pump coronary surgery: The effect on stroke. Journal of Thoracic and Cardiovascular Surgery 129 (2) 307–313.	Follow up = not reported	irrespective of the severity of aortic disease or the method of aortic screening. This technique is recommended whenever technically feasible.	
Lu JC, Grayson AD, and Pullan DM (2005) On-pump versus off-pump surgical revascularization for left main stem stenosis: risk adjusted outcomes. Annals of Thoracic Surgery 80 (1) 136–142.	n = 1197 Follow up = 2 years	After risk adjustment, patients with critical left main stem stenosis can undergo off-pump coronary surgery safely, with results comparable with on-pump coronary surgery.	Larger studies are included in table 2
Manabe S, Fukui T, Miyajima, K et al. (2009) Impact of proximal anastomosis procedures on stroke in off-pump coronary artery bypass grafting. Journal of Cardiac Surgery 24 (6): 644–650	n = 535 Follow up = not reported	Aortic clamping could be performed safely in patients with normal or mild atherosclerotic aorta. In patients with moderate atherosclerosis, the result of an anastomosis may need a further investigation.	Larger studies are included in table 2
Masuhara H, Watanabe Y, Shiono N et al. (2005) A case report of emergency off-pump CABG in an aged patient with ACS renewing ventricular fibrillation. Annals of Thoracic & Cardiovascular Surgery 12 (3) 219–222.	n = 1 Follow up = 2 months	We think that off-pump CAB is an effective surgical technique for coronary revascularisation for emergency or serious cases involving elderly patients.	Larger studies are included in table 2
Massoudy P, Thielmann, M Szabo, A et al. (2006) Aortocoronary Shunting during off pump coronary artery bypass surgery as acute reperfusion strategy in ST-elevation myocardial infarction. Annals of Thoracic Surgery 82 (4): 1521–1523.	n = 1 Follow up = 3 days	Under the protection of the aortocoronary shunt, the left internal thoracic artery was harvested and was thereafter anastomosed to the left anterior descending artery. The patient had an uneventful postoperative recovery	Larger studies are included in table 2
Matsuda N, Kamihira S, Kanaoka Y et al. (2005) Off-pump axillo-	n = 1	The off-pump axillo-coronary artery bypass grafting seemed to be an	Larger studies are included in table 2

coronary artery bypass grafting with porcelain aorta. Journal of Cardiac Surgery 20 (6) 586–588.	Follow up = 2.2 months	appropriate procedure for coronary revascularization with severely diseased ascending aorta.	
Matsuura K, Kobayashi J, Tagusari O, et al. (2004) Rationale for off-pump coronary revascularization to small branches - Angiographic study of 1,283 anastomoses in 408 patients. Annals of Thoracic Surgery 77 (5) 1530–1534.	n = 408 Follow up = not reported	Off-pump CAB to small coronary artery branches with arterial grafts provided satisfactory graft patency and stenosis free rates	Larger studies are included in table 2
Matsuura K, Kobayashi J, Bando K et al. (2006) Redo off-pump coronary bypass grafting with arterial grafts for Kawasaki disease. Heart & Vessels 21 (6) 361–364.	n = 1 Follow up = 18 months	Off-pump total arterial revascularization is a safe and less invasive procedure at the time of redo operation, even for patients with Kawasaki disease.	Larger studies are included in table 2
Matsuura K, Imamaki M, Ishida A et al. (2009) Off-pump coronary artery bypass grafting for poorly controlled diabetic patients. Annals of Thoracic & Cardiovascular Surgery 15 (1) 18–22.	n = 101 Follow up = 2.2	Off-pump CAB is feasible in patients having poorly controlled diabetes mellitus, and their condition does not compromise the surgical outcome.	Larger studies are included in table 2
Minato N, Katayama Y, Sakaguchi M et al. (2006) Perioperative coronary artery spasm in off-pump coronary artery bypass grafting and its possible relation with perioperative hypomagnesemia. Annals of Thoracic & Cardiovascular Surgery 12 (1) 32–36.	n = 3 Follow up = 30 to 75 days	Hypomagnesemia, one of the triggers of coronary artery spasm, is very common in off-pump CAB. We strongly recommend the correction of hypomagnesemia during and after off-pump CAB for the prevention of perioperative coronary artery spasm.	Larger studies are included in table 2
Mishra M, Shrivastava S, Dhar A et al. (2003) A prospective evaluation of hemodynamic instability during off-pump coronary artery bypass surgery.	n = 500 Follow up = not reported	Patients with low left ventricular ejection fraction < 25%, myocardial infarction of <1-month duration, congestive heart failure, or preoperative hemodynamic instability constitute the high-risk	Larger studies are included in table 2

Journal of Cardiothoracic & Vascular Anesthesia 17 (4) 452–458.		group for off-pump CAB.	
Nakajima H, Kobayashi J, Funatsu T et al. (2007) Predictive factors for the intermediate-term patency of arterial grafts in aorta no-touch off-pump coronary revascularization. European Journal of Cardio-Thoracic Surgery 32 (5) 711–717.	n = 677 Follow up = 29 months	For the left anterior descending artery, the results of graft flow in sequential grafting or composite grafting with two distal anastomoses were comparable with that in individual grafting.	Larger studies are included in table 2
Nakano J, Okabayashi H, Hanyu M et al. (2008) Risk factors for wound infection after off-pump coronary artery bypass grafting: should bilateral internal thoracic arteries be harvested in patients with diabetes? Journal of Thoracic & Cardiovascular Surgery 135 (3) 540–545.	n = 1500 Follow up = not reported	Factors for wound infection after off-pump CAB grafting are comparable with those previously reported for conventional bypass grafting.	Larger studies are included in table 2
Naseri E and Sevinc M (2003) Off-Pump Coronary Bypass through Very Limited Sternotomy. Heart Surgery Forum 6 (4) E63–E67.	n = 76 Follow up = 27 months	Early and midterm results are comparable with those of classic methods of myocardial revascularization. Conversion to full sternotomy is quite easy and safe, should the necessity arise.	Larger studies are included in table 2
Nomura F, Mukai S, Tamura K et al. (20020 Cost performance and efficacy of off-pump coronary artery bypass grafting. Hiroshima Journal of Medical Sciences 51 (4) 85–87.	n = 64 Follow up = 14 days	Graft patency rates were similar in both groups (98% in off-pump CABG vs 98% in on-pump CABG).	Larger studies are included in table 2
Ogiwara M, Hojo H, Ozaki M et al. (2006) Off-pump coronary artery bypass grafting for a patient with anomalous origin of the	n = 1 Follow up = 13 days	This case required coronary revascularisation because of the atherosclerotic LAD stenosis as a collateral source of the right coronary	Larger studies are included in table 2

right coronary artery from the pulmonary artery. Annals of Thoracic & Cardiovascular Surgery 12 (6) 432–434.		artery.	
Ono M and Michler RE (2003) Beating heart coronary artery bypass surgery after orthotopic heart transplantation. Journal of Cardiac Surgery 18 (6) 545–550.	n = 1 Follow up = 13 months	Coronary angiography 3 months after the surgery revealed a widely patent left internal mammary artery to left anterior descending artery bypass. He is alive and symptom-free more than 1 year after his surgery.	Larger studies are included in table 2
Onorati F, De Feo M, Sante P et al. (2006) Perioperative optic neuropathy following off-pump coronary artery bypass grafting. Journal of Cardiovascular Surgery 47 (5): 585–587.	n = 1 Follow up = 24 months	We report here a very rare case of perioperative optic neuropathy following off-pump surgery in a patient with severe coronary disease and multi-organ comorbidities.	Larger studies are included in table 2
Osaka S, Ohsawa H, and Nabuchi A (2002) Redo off-pump coronary artery bypass grafting for high risk hemodialysis patients. Journal of Cardiac Surgery 17 (5) 383–386.	n = 2 Follow up = 4 to 6 months	Redo off-pump CAB can be performed with minimal dissection via median sternotomy.	Larger studies are included in table 2
Paulitsch FS, Schneider D, Sobel BE et al. (2009) Hemostatic changes and clinical sequelae after on-pump compared with off-pump coronary artery bypass surgery: A prospective randomized study. Coronary Artery Disease 20 (2) 100–105.	n = 92 Follow up = 1 year	On-pump surgery was associated with biochemical evidence of a prothrombotic state early after surgery but no greater incidence of thrombotic events was observed.	Larger studies are included in table 2
Poston R, White C, Read K et al. (2004) Virchow triad, but not use of an aortic connector device, predicts early graft failure after off-pump coronary bypass. Heart Surgery Forum 7	n = 91 Follow up = not reported	The perioperative combination of platelet hyperreactivity, marginal graft flow, and endothelial disease proved to be highly predictive of early graft failure as seen with postoperative computed tomographic angiography.	Larger studies are included in table 2

(5) E428–E433.			
Poston RS, White C, Gu J et al. (2006) Aprotinin shows both hemostatic and antithrombotic effects during off-pump coronary artery bypass grafting. Annals of Thoracic Surgery 81 (1) 104–111.	n = 60 Follow up = 10 to 20 months	Aprotinin reduced perioperative bleeding after off-pump CABG.	Larger studies are included in table 2
Raja SG, Siddiqui H, Ilsley CD and Amrani M (2009) In-hospital outcomes of off-pump multivessel total arterial and conventional coronary artery bypass grafting: single surgeon, single center experience.[see comment]. Annals of Thoracic Surgery 88 (1) 47–52.	n = 1386 Follow up = not reported	Off-pump multivessel total arterial grafting can be performed safely with superior in-hospital outcomes compared with off-pump conventional CAB grafting.	Larger studies are included in table 2
Rauch ED, Leach C, Barnes T et al. (2007) Intraoperative assessment and quantification of coronary artery graft patency performed on or off cardiopulmonary bypass. Journal of Extra-Corporeal Technology 39 (2) 75–81.	n = 74 Follow up = not reported	Although we were able to show some significance in the mean flow data supporting increased graft flow with the on-pump technique, we were not able to show an overall increase in all recorded flow characteristics to support one method over another	Larger studies are included in table 2
Reuthebuch O, Haussler A, Genoni M et al. (2004) Novadaq SPY: Intraoperative Quality Assessment in Off-Pump Coronary Artery Bypass Grafting. Chest 125 (2) 418–424.	n = 38 Follow up = not reported	This study supports the clinical utility of a indocyanine green based imaging system for the assessment of the quality of bypass grafts, which appears to be safe and simple to use.	Larger studies are included in table 2
Saba D, Ener S, Bicer M et al. (2004) Off-pump bypass grafting in patients with significant left main coronary artery stenosis. Heart & Vessels 19 (1) 8–12.	n = 200 Follow up = 2 months minimum	In significant left main coronary artery stenosis coronary bypass on the beating heart is a safe and effective alternative to the conventional method with the same or better early results. The long-term results need to be	Larger studies are included in table 2

		evaluated.	
Sakamoto S, Ochi M, Bessho R et al. (2003) Perioperative myocardial infarction in patients undergoing off-pump coronary artery bypass grafting Japanese Journal of Thoracic & Cardiovascular Surgery 51 (8): 393–396.	n = 1 Follow up = not reported	There was no ischaemic episode during operation. Coronary artery spasms and/or intracoronary thrombus formation may have been causes of these events.	Larger studies are included in table 2
Sakao T, Kashu Y, Nakagawa H et al. (2003) Off-pump coronary artery bypass grafting in two renal transplant patients. Japanese Journal of Thoracic & Cardiovascular Surgery 51 (12) 678–680.	n = 2 Follow up =1 month	Off-pump CAB graft for a renal transplant patient was safe and useful since it is a less invasive procedure and easily managed perioperatively.	Larger studies are included in table 2
Shaker W, Farhat F, Chuzel M, et al. (2003) Off-pump coronary bypass surgery for left main coronary artery stenosis 10 years after heart transplantation: case report. Journal of Heart & Lung Transplantation 22 (10) 1178–1180.	n = 1 Follow up = 5 months	A patient with asymptomatic left main coronary artery stenosis 10 years after heart transplantation was treated successfully with off-pump coronary bypass surgery using both mammary arteries.	Larger studies are included in table 2
Sharony R, Bizekis CS, Kanchuger M et al. (2003) Off-pump coronary artery bypass grafting reduces mortality and stroke in patients with atheromatous aortas: a case Circulation 108 Suppl-20.	n = 422 Follow up = 36 months	Off-pump CAB surgery in patients with severe atheromatous aortic disease is associated with lower risk of death, stroke and complications and improved mid-term survival.	Larger studies are included in table 2
Sharony R, Grossi EA, Saunders P et al. (2004) Propensity case-matched analysis of off-pump coronary artery bypass grafting in patients with atheromatous Journal of Thoracic & Cardiovascular Surgery 127 (2) 406–413.	n = 490 Follow up = 3 years	Patients with severe atherosclerotic aortic disease who undergo off-pump CAB grafting have a significantly lower prevalence of hospital mortality, perioperative stroke, and overall complications than matched patients who underwent coronary artery	Larger studies are included in table 2

		bypass grafting with cardiopulmonary bypass.	
Shapira OM, Natarajan, V, Kaushik S et al. (2004) Off-pump versus on-pump reoperative CABG via a left thoracotomy for circumflex coronary artery revascularization. Journal of Cardiac Surgery 19 (2) 113–119.	n = 32 Follow up = 33 months	The off-pump CAB technique is associated with reduced blood product utilization and shorter ICU and hospital length of stay.	Larger studies are included in table 2
Shim JK, Choi YS, Yoo KJ et al (2009) Carbon dioxide embolism induced right coronary artery ischaemia during off-pump obtuse marginalis artery grafting. European Journal of Cardio-Thoracic Surgery 36 (3): 598–599.	n = 1 Follow up =not reported	In case of massive embolism, needle aspiration of the gas should also be considered.	Larger studies are included in table 2
Spiess BD, DeAnda A, McCarthy HL et al. (2006) Off-pump coronary artery bypass graft surgery anticoagulation with bivalirudin: A patient with heparin-induced thrombocytopenia syndrome type II and renal failure. Journal of Cardiothoracic and Vascular Anesthesia 20 (1) 106-111	n = 1 Follow up = 2 weeks	Authors report a CABG case with presumed Heparin induced thrombocytopenia syndrome type II with renal failure where bivalirudin was used as the anticoagulant.	Larger studies are included in table 2
Tagusari O, Kobayashi J, Bando K et al. (2004) Total arterial off-pump coronary artery bypass grafting for revascularization of the total coronary system: clinical outcome and angiographic evaluation. Annals of Thoracic Surgery 78 (4) 1304–1311.	n = 382 Follow up = not reported	Total arterial off-pump CAB yielded good clinical results and an excellent patency rate of revascularisation for the total coronary system.	Larger studies are included in table 2
Tjomsland O, Wiseth R, Wahba A et al. (2003) Intraoperative color	n = 20	Intraoperative color Doppler ultrasound allows a detailed evaluation of left internal	Larger studies are included in table 2

Doppler ultrasound assessment of anastomoses of the left internal mammary artery to the left anterior descending coronary artery during off-pump coronary artery bypass surgery correlates with angiographic evaluation at the 8-month follow-up. Heart Surgery Forum 6 (5) 375–379.	Follow up = 245 days	mammary artery to the left anterior descending coronary artery anastomoses during off-pump surgery, and the results correlate significantly with those of angiographic evaluation after 8 months.	
Troise G, Brunelli F, Cirillo M et al. (2002) Off-pump coronary surgery in a single center experience: From selective to systematic use. Italian Heart Journal 3 (8) 446–454.	n = 1221 Follow up = 14 to 29 months	The increase in the use of off-pump CAB up to its systematic employment is feasible. The early and intermediate results are satisfactory.	Studies with longer follow up are included in table 2
Vaidyanathan KR, Sundaramoorthi T, Byalal JR et al. (2006) Lower extremity compartment syndrome after off-pump aortocoronary bypass. Journal of Thoracic & Cardiovascular Surgery 131 (5): 1173–1174.	n = 1 Follow up =not reported	Periodic examination of the vein donor limb for at least 24 hours to detect limb swelling or tenderness on passive dorsiflexion is essential.	Larger studies are included in table 2
Vedin J, Nyman, H., Ericsson, A et al (2006) Cognitive function after on or off pump coronary artery bypass grafting. European Journal of Cardio-Thoracic Surgery 30 (2) 305–310.	n = 70 Follow up = 6 months	This prospective, randomised study showed no differences in post-operative cognitive function after on-pump compared with off-pump CAB grafting in low-risk patients.	Larger studies are included in table 2
Virani SS, Lombardi P, Tehrani H et al. (2005) Off-pump coronary artery grafting in patients with left main coronary artery disease. Journal of Cardiac Surgery 20 (6) 537–541.	n = 95 Follow up = not reported	Patients with Left main coronary artery disease can undergo off-pump CAB grafting safely and effectively despite reduced left ventricular ejection fraction.	Larger studies are included in table 2
Vural KM, Iscan ZH, Kunt A et al. (2005) Off-pump coronary artery bypass grafting: long	n = 265 Follow up = 4.2 years	Probably the best candidates for off-pump CAB are those having target vessels of good	Larger studies are included in table 2

term angiographic results. Journal of Cardiac Surgery 20 (2) 153–159.		caliber and quality, and high-grade stenoses. Postoperative lipid-lowering therapy seems to be prudential.	
Walther T, Dahnert I, Kiefer H et al. (2005) Beating heart off-pump myocardial revascularization in an infant. Annals of Thoracic Surgery 79 (6) 2151–2153.	n = 1 Follow up = 15 days	Closure of the left main stem and left internal mammary artery-left anterior descending CAB grafting were performed successfully with the heart beating.	Larger studies are included in table 2
Wolf LG, Abu-Omar, Y, Choudhary BP et al (2007) Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary surgery: the effect of an aortic side-biting clamp and two clampless devices. Journal of Thoracic & Cardiovascular Surgery 133 (2) 485–493.	n = 42 Follow up = not reported	Avoidance of aortic side clamping results in a significant reduction in the proportion of solid microemboli detected with transcranial Doppler.	Larger studies are included in table 2
Yotsumoto G, Masuda, H, Toyokawa K et al (2005) Off-pump coronary artery bypass grafting in a patient with congenital factor V deficiency: report of a case. Surgery Today 35 (2) 142–144.	n = 1 Follow up = 3 weeks	A patient with severe factor V deficiency underwent successful off-pump CAB grafting with a transfusion of fresh-frozen plasma.	Larger studies are included in table 2

Appendix B: Related NICE guidance for off-pump coronary artery bypass grafting

Guidance	Recommendations
Technology appraisals	**Drug-eluting stents for the treatment of coronary artery disease NICE technology appraisal 152 (2008)** 1.1 Drug-eluting stents are recommended for use in percutaneous coronary intervention for the treatment of coronary artery disease, within their instructions for use, only if: • the target artery to be treated has less than a 3-mm calibre or the lesion is longer than 15 mm, and • the price difference between drug-eluting stents and bare-metal stents is no more than £300.

Appendix C: Literature search for off-pump coronary artery bypass grafting

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	9/12/2009	Issue 4, 2009	2
Database of Abstracts of Reviews of Effects – DARE (CRD website)	9/12/2009	N/A	9
HTA database (CRD website)	9/12/2009	N/A	0
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	9/12/2009	Issue 4, 2009	65
MEDLINE (Ovid)	9/12/2009	1950 to November Week 3 2009	182
MEDLINE In-Process (Ovid)	9/12/2009	December 08, 2009	6
EMBASE (Ovid)	9/12/2009	1980 to 2009 Week 49	182
CINAHL (NLH Search 2.0)	9/12/2009	N/A	246
BLIC (Dialog DataStar)	9/12/2009	N/A	0
General internet search	9/12/2009	None found	

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

# ▲	Searches	Results
1	Coronary Artery Bypass, Off-Pump/	1454
2	("off-pump" adj3 coronar* adj3 arter* adj3 bypass*).tw.	1638
3	OPCAB.tw.	798
4	(beat* adj3 heart* adj3 coronar* adj3 arter* adj3 bypass*).tw.	100
5	((graft* or immobili?ation or stabili?ation) adj3 "off pump").tw.	298
6	(("off pump" or "beating heart") adj3 bypass*).tw.	2066
7	or/1-6	2778
8	Coronary Vessel Anomalies/	5860
9	Atherosclerosis/	10235
10	atheroma*.tw.	7844
11	atheroscleros*.tw.	60395
12	(arterial* adj3 fatty* adj3 streak*).tw.	10

13	Coronary Stenosis/	5496
14	(coronar* adj3 stenosis*).tw.	6777
15	or/8-14	85315
16	7 and 15	232
17	animals/ not humans/	3432406
18	16 not 17	221
19	limit 18 to ed=20030101-20091209	204
20	limit 19 to english language	182