

REVIEW

Off-pump coronary artery bypass graft surgery: the incidence of postoperative atrial fibrillation

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Heart 2003;89:1134–1137

Atrial fibrillation (AF) occurs in one quarter to one third of patients after coronary artery bypass graft surgery (CABG). Conventional CABG uses cardiopulmonary bypass, a process that is itself associated with a systemic vascular inflammatory response that contributes to postoperative morbidity. The avoidance of cardiopulmonary bypass is associated with a significant reduction in the inflammatory response and in the release of markers of myocardial necrosis when compared with conventional CABG. There is speculation that off-pump CABG may reduce the incidence of postoperative AF through reduced trauma, ischaemia, and inflammation. Current data, however, do not emphatically answer the question of whether the incidence of post-CABG AF is reduced by off-pump surgery. The evidence from both observational and randomised studies is conflicting and many studies have weaknesses in design, conduct, or interpretation. It remains an attractive hypothesis that postoperative AF is reduced by off-pump CABG but more robust data are required.

change in autonomic tone, or the response to cardiopulmonary bypass (CPB), may precipitate AF in these patients.

Conventional CABG employs CPB during the period of cardiac arrest. This provides for extracorporeal oxygenation of blood before returning it to the systemic circulation, thus ensuring adequate delivery to the vital organs. CPB is itself associated with a systemic inflammatory response syndrome that contributes to postoperative morbidity.⁴ Post-pump syndrome is characterised by leucocytosis, increased capillary permeability, accumulation of interstitial fluid, and organ dysfunction. It is thought to be triggered by surgical trauma, lung reperfusion, and contact of blood with the “foreign” extracorporeal bypass circuit.

Currently only circumstantial evidence suggests a causal relation between CPB and postoperative AF, a minority of investigators having reported an association between bypass time and post-CABG AF.⁵ Nevertheless, it remains an attractive hypothesis that the avoidance of CPB will reduce the incidence of post-CABG AF.

DOES OFF-PUMP CABG REDUCE THE INCIDENCE OF POST-CABG AF? THE TRIAL EVIDENCE

There is considerable interest in beating heart surgery without CPB and minimally invasive direct coronary artery bypass (MIDCAB), both of which may reduce postoperative morbidity. Off-pump CABG is associated with a significant reduction in the inflammatory response⁶ and in the release of markers of myocardial necrosis⁷ compared with conventional CABG. Furthermore, there are now data assessing the incidence of AF in patients revascularised by these techniques (tables 1 and 2).^{8–12}

In two series, post-CABG AF occurred in 18 (5.9%) of 306 patients who underwent left internal mammary artery grafting to the left anterior descending artery by MIDCAB²³ and was recorded in only 34 (1.7%) of 2052 patients who had off-pump CABG by median sternotomy.²⁵ In a study of patients who underwent CABG by MIDCAB (n = 93) or conventional operation (n = 74), AF was less frequent (7% v 31%, respectively; p < 0.05) in the group without CPB.¹⁰ By contrast, different series have reported rates of AF

Approximately 27 000 people in the UK and 500 000 people in the USA undergo coronary artery bypass graft surgery (CABG) annually, 25–30% of whom develop atrial fibrillation (AF) postoperatively. AF is associated with increased morbidity and expenditure, and prolonged hospital stay after CABG.¹ Advances in surgical techniques have not been accompanied by a decrease in the incidence of post-CABG AF. However, the use of “off-pump” CABG may provide a novel solution to this problem. This review analyses the current evidence regarding the incidence of AF after off-pump CABG.

PATHOGENESIS OF POST-CABG AF: A ROLE FOR THE “POST-PUMP SYNDROME”?

The pathogenesis of post-CABG AF is incompletely understood. Evidence suggests that the patients at greatest risk of developing the arrhythmia have an identifiable electrophysiological substrate.² The nature of this substrate may be slow atrial conduction or dispersion of atrial refractoriness.³ A number of perioperative factors, such as inadequate myocardial protection, electrolyte imbalance, β blocker withdrawal,

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Accepted 7 April 2003

Table 1 Incidence of AF after conventional and minimally invasive direct CABG

Study, year (reference)	Incidence of postoperative AF		p Value
	CPB	Non-CPB	
Allen 1997* (8)	7/12 (58%)	0/23 (0%)	0.0001
Collard 1997 (9)	NA	1/10 (10%)	NA
Allen 1998 (10)	23/74 (31%)	6/93 (7%)	<0.05
Calafiore 1998 (11)	NA	35/434 (8%)	NA
Jansen 1998 (12)	NA	5/54 (9.3%)	NA
Tamis 1998 (13)	11/33 (33%)	11/42 (26%)	NS
Arom 1999 (14)	39/243 (16%)	8/44 (18%)	NA
Cohn 1999 (15)	11/55 (20%)	13/55 (24%)	0.6
Abreu 1999 (16)	192/747 (26%)	4/34 (12%)	0.06
Turner Jr 1999 (17)	NA	5/100 (5%)	NA
Siebert 2000 (18)	7/39 (18%)	6/24 (25%)	NS
Stamou 2000 (19)	NA	40/292 (14%)	NA
Koutlas 2000† (20)	57/220 (26%)	14/53 (26%)‡	NS
d'Amato 2000 (21)	14/42 (28%)	4/96 (4%)	0.003
Tamis-Holland 2000 (22)	42/108 (39%)	23/101 (23%)	0.02
Cremer 2000 (23)	NA	18/306 (5.9%)	NA
Hravnak 2001 (24)	238/720 (33.1%)	22/94 (23.4%)	0.059

*Single vessel repeat coronary artery bypass graft surgery; †≥75 years; ‡majority by minimally invasive direct coronary artery bypass.
AF, atrial fibrillation; CPB, cardiopulmonary bypass; NA, not applicable.

of up to 37% despite no CPB,²⁶ while other observational studies have shown no difference in AF incidence post-CABG with and without CPB.^{16–20}

Theoretically, any reduction in AF incidence after off-pump CABG may be attributed to the less invasive nature of MIDCAB procedures than of median sternotomy rather than

to the absence of CPB. In 969 patients who underwent CABG without CPB, for example, MIDCAB was associated with a lower incidence of AF (14% v 25%; odds ratio 0.4, 95% confidence interval 0.3 to 0.7; p < 0.001) than a median sternotomy approach.¹⁹ Specific information about the impact of CPB on postoperative AF therefore comes from studies

Table 2 Incidence of AF after conventional and off-pump CABG by median sternotomy

Study, year (reference)	Incidence of postoperative AF		p Value
	CPB	Non-CPB	
Collard 1997 (9)	NA	22/66 (33%)	NA
Jansen 1998 (12)	NA	7/46 (15.2%)	NA
Tasdemir 1998 (25)	NA	34/2052 (1.7%)	NA
Saatvedt 1999 (26)	248/685 (36%)	7/19 (37%)	NS
Spooner 1999 (27)	NA	44/331 (13.3%)*	NA
Boyd 1999 (28)	17/60 (28.3%)	3/30 (10%)†	<0.05
Ardehali 1999 (29)	NA	5/26 (19%)	NA
Arom 1999 (14)	39/243 (16%)	8/62 (13%)	NS
Cartier 2000 (30)	580/1870 (31%)	90/300 (30%)	0.8
Siebert 2000 (18)	7/39 (18%)	7/24 (29%)	NS
Stamou 2000 (19)	NA	166/677 (25%)	NA
Stamou 2000*** (31)	12/41 (29%)	13/91 (14%)‡	0.04
Ascione 2000 (32)	39/100 (39%)	8/100 (8%)	0.001
Arom 2000 (33)	721/3171 (23%)	50/350 (14%)	<0.001
Kshetry 2000 (34)	131/609 (21.5%)	24/135 (17.8%)	NS
Hart 2000 (35)	NA	236/1582 (14.9%)§	NA
Arom 2000¶ (36)	31/132 (23%)	6/45 (13.3%)	0.154
Hernandez 2000 (37)	102/445 (22.9%)	63/332 (19.0%)	NS
Omeroglu 2000 (38)	NA	5/70 (7.1%)	NA
Bedi 2000 (39)	NA	1/100 (1%)	NA
Kilger 2001 (40)	9/53 (17%)	2/50 (4%)	<0.05
Czerny 2001 (41)	7/40 (17.5%)	5/40 (12.5%)	NS
Bull 2001 (42)	7/40 (18%)	7/40 (18%)	NS
Yeatman 2001** (43)	38/312 (12.2%)	9/75 (12%)	0.95
Bowles 2001 (44)	24/70 (34%)	22/67 (33%)	NS
Calafiore 2001 (45)	111/924 (12%)	110/919 (12%)	NS
Siebert 2001 (46)	64/650 (9.8%)	12/118 (10.2%)	0.9††
Arom 2001‡‡ (47)	NA	56/342 (16.4%)	NA
Puskas 2001 (48)	158/1000 (15.8%)	25/200 (12.5%)	0.28
Demers 2001§§ (49)	268/497 (54%)	41/98 (42%)	0.05
Lund 2001 (50)	109/368 (29.6%)	37/165 (22.4%)	NS
Van Dijk 2001 (51)	29/139 (21%)	28/142 (20%)	0.79
Al-Ruzzeah 2001¶¶ (52)	35/84 (41%)	16/56 (29%)	0.15

*Mixed approaches; †>70 years old and 93% by median sternotomy; ‡56% by median sternotomy; §83% by median sternotomy; ¶ejection fraction ≤30%; **left main stenosis ≥50%; ††AF incidence on intensive care unit (mean two days); ‡‡ejection fraction >30%; §§≥70 years; ¶¶≥75 years; ***single vessel repeat coronary artery bypass graft surgery.

comparing patients undergoing median sternotomy with and without CPB. Thus, AF occurred in 23% of 3171 patients who underwent conventional CABG compared with 14% of 350 off-pump operations performed through sternotomy ($p < 0.001$).³³ Objective comparison is, however, difficult since the off-pump patients received fewer grafts, had shorter surgery, and were ventilated for a shorter period. Furthermore, in other studies, the incidence of AF was not significantly different in groups undergoing CABG by median sternotomy with and without CPB.^{26,48}

The importance of considering differences in clinical characteristics is illustrated by a recent study in which the incidence of post-CABG AF was significantly lower (23% *v* 39%; $p = 0.02$) among 101 MIDCAB patients than in 108 on-pump patients.²² The MIDCAB patients were younger, had a lower frequency of previous cardiac surgery, had less extensive coronary disease, received fewer grafts, and had a shorter postoperative hospital stay. After adjustment for these differences, surgical method was no longer a significant predictor of AF.

To elucidate the role of CPB properly in post-CABG AF, randomised data are required. In one study, 200 low risk patients were randomly assigned to off-pump or conventional CABG.³² Sustained AF (> 10 minutes) was significantly less common (8% *v* 39%; $p = 0.001$) in the off-pump group. Indeed CPB was the only independent predictor of postoperative AF. These data, however, contrast with those from a more recent trial in which 281 patients undergoing first, elective, isolated CABG were randomly assigned to on- or off-pump surgery.⁵¹ All patients received sotalol prophylaxis. Off-pump CABG resulted in reduced creatine kinase MB fraction release, reduced use of blood products, and a shorter hospital stay compared with on-pump surgery, but nevertheless the incidence of AF (20% *v* 21%, respectively; $p = 0.79$) was similar.

DISCUSSION

Post-CABG AF continues to affect morbidity, hospital stay, and financial resources. There is speculation that off-pump CABG may reduce the incidence of AF, but current data do not answer this hypothesis. The evidence is conflicting. Interpretation of studies is confounded by patient selection, inappropriate control groups, and poorly defined arrhythmia monitoring.

Alternative strategies for reducing both the inflammatory response to CPB and the incidence of post-CABG AF exist. β Blockers are generally accepted to prevent AF.⁵³ Some studies have reported a reduction in the serum concentration of inflammatory markers after CPB using heparin coated extracorporeal circuits, or by high dose aprotinin or prednisolone.⁵⁴ Whether these findings translate into clinical benefit, specifically a decrease in the incidence of post-CABG AF, remains uncertain.

Conclusion

Off-pump techniques offer several potential advantages over conventional CABG (shorter operation times, more rapid recovery times, reduced neurocognitive impairment, reduced need for blood products). It is uncertain whether a reduction in the incidence of postoperative AF can be added to this list. More robust data are required.

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IMAGES IN CARDIOLOGY.....

Life threatening total occlusion of the left coronary artery after acetylcholine infusion

A 44 year old woman was referred to the hospital with anginal complaints and ST segment changes during exercise. A coronary angiogram was performed, but no stenoses were found. As her complaints persisted the question arose as to whether this could be caused by coronary spasm. Therefore it was decided to perform an acetylcholine provocation test. Acetylcholine was infused into the left main artery at a rate of 0.22 µg/min. After two minutes, the patient experienced severe anginal pain and the ECG showed ST segment elevations. Another angiogram was taken and revealed

severe coronary spasm of both the left anterior descending (LAD) and the circumflex (CX) coronary arteries (below left). A bolus of glyceryl trinitrate was given intracoronary to achieve vasodilation. This action was repeated, but with no satisfactory result. Subsequently, an intracoronary bolus of atropine (500 µg) was given as a last resort to terminate the spasm. After one dose of atropine the CX was open again, whereas the distal LAD remained closed (below centre). A second bolus was needed to normalise the angiogram (below right) as well as the ECG. Although a slight increase in troponin was found after the procedure,

no major complications occurred and the patient was discharged from hospital two days later.

This case shows that life threatening coronary spasms can occur during acetylcholine infusion in patients with "normal" coronary arteries. More important, glyceryl trinitrate is not always capable of reversing the evoked coronary spasm. Intracoronary atropine infusion may establish a satisfying vasodilating effect in these cases.

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