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Retaining the Aortic Fat Pad During Cardiac Surgery Decreases Postoperative Atrial Fibrillation

Dr. Davis

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ABSTRACT

Background: Atrial arrhythmias are a common and serious complication of cardiac surgical procedures. Reports describing pericardiac neurogenic tissue led us to hypothesize that removal of the aortic fat pad could cause an autonomic imbalance and contribute to atrial arrhythmias following cardiac surgery.

Methods: Patients (n = 131) underwent either conventional cardiopulmonary bypass surgery (CPB) or off-pump coronary artery bypass (OPCAB) surgery. The aortic fat pad was either left intact or removed. The incidence of *de novo* atrial arrhythmias during the patient's hospital stay was tabulated. Patients with peri-operative myocardial infarction or pre-existing atrial or supraventricular arrhythmias were excluded.

Results: Demographics, preoperative medications, ASA and NYHA classifications, and complication rates (other than for atrial arrhythmias) did not differ among the groups. The STS-predicted mortality was higher in the CPB/Fat-Pad-Removed group (2.23 ± 1.89) than in either the OPCAB/Fat-Pad-Intact (1.09 ± 0.80) or OPCAB/Fat-Pad-Removed (1.02 ± 0.62) groups ($p < 0.05$). Atrial arrhythmias were present in 19 of 131 patients (14.5%). Logistic regression demonstrated a significantly elevated atrial arrhythmia rate when the fat pad was removed (odds ratio = 3.49, 95% bounds 1.09 to 11.18, $p = 0.035$). Neither the pump status nor the cross product of pump status by fat pad status were significant in this pilot study.

Conclusions: Retaining the aortic fat pad during coronary artery bypass surgery is correlated with a decreased incidence of postoperative atrial arrhythmias.

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INTRODUCTION

Atrial arrhythmias are the most common complication of cardiac surgical procedures today [Creswell 1999]. There are extensive clinical and experimental studies that are designed to prevent or treat these arrhythmias; many of the studies have conflicting results [Hogue 2000]. The majority of cardiac interventions are after the occurrence of new onset of atrial fibrillation; they affect patient morbidity, are costly, and tend to prolong hospital stay.

Cox [1999] has suggested that patients who are candidates for cardiac surgery may be categorized into 3 groups reflecting their vulnerability to develop postoperative atrial fibrillation. Five percent of patients who undergo cardiac or noncardiac surgery will develop postoperative atrial fibrillation. Approximately 65% will not develop atrial fibrillation after cardiac surgery, irrespective of the procedure performed. The remaining 30–35% of patients have an underlying propensity to develop postoperative atrial fibrillation regardless of the type of surgery performed. Given the number of cardiac procedures performed yearly, the number of patients potentially affected with postoperative atrial fibrillation could be close to 150,000/year.

There are early reports from animal studies [Chiou 1977, Randall 1983, Randall 1985, Burkholder 1992] that describe neurogenic tissue in pericardiac areas, including the ascending aortic fat pad and fatty tissue between the aorta and pulmonary artery. These studies have been extended to humans by Armour et al. [1997] who reported over 14,000 neurons in the heart with most ganglia located on the epicardial surface in a complex array of fat pads. More recently, an enormously complex neural network in the guinea pig heart has been shown [Horackova 1999]

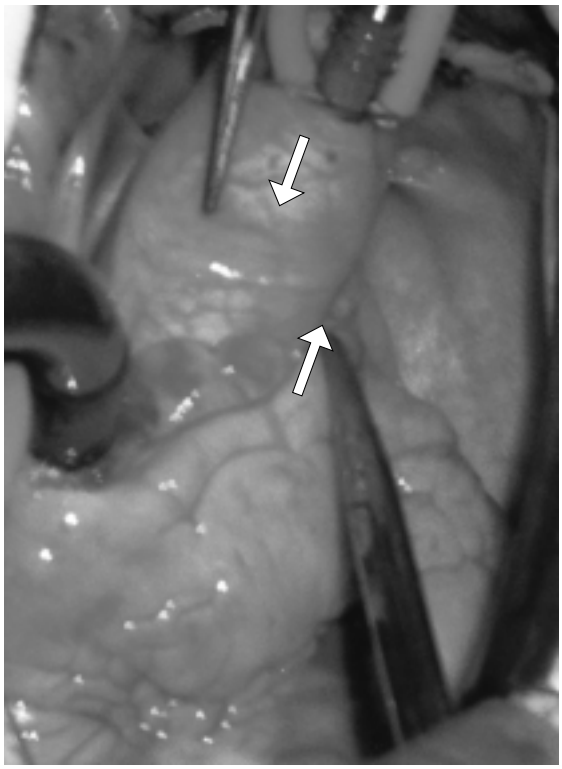

Figure 1. Exposed heart showing fat pad overlying aorta with contiguous aorto-pulmonary tissue.

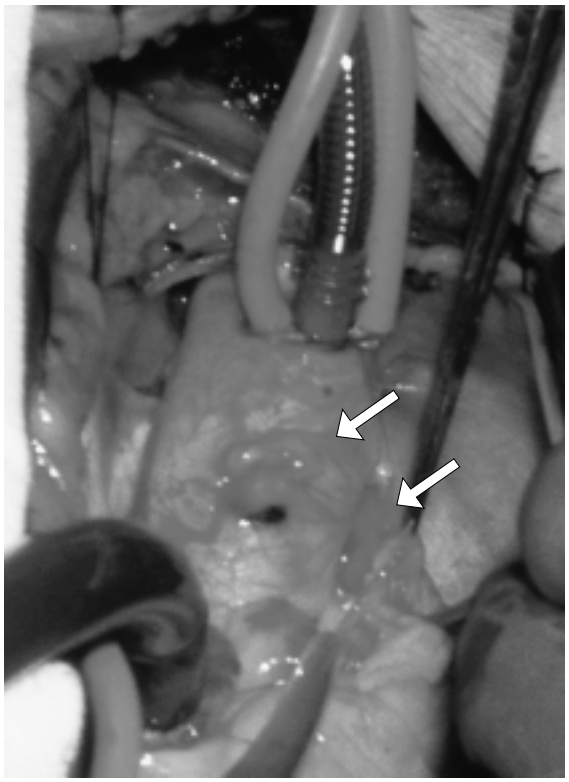

Figure 2. Aorto-pulmonary tissue divided, and aortic fat pad dissected prior to removal.

which also seems to be present in the human heart [Armour, personal communication]. If normal input to these highly selective intra- and pericardiac neurogenic pathways is altered, then discharge patterns of the autonomic nervous system could be altered and could lead to dispersion of refractoriness and thus contribute to arrhythmias [Cox 1991, Cox 1993, Konings 1994].

Traditionally, the aortic fat pad is removed (Figures 1 and 2, ◎) during cardiopulmonary bypass (CPB) to more easily expose the ascending aorta for aortic cannulation, vent, and cardioplegic catheter placement, and for aortic cross clamping. The majority or the entire fat pad between the aorta and pulmonary artery, as well as its extension onto the anterior surface of the ascending aorta, is excised completely with scissors and cautery. We postulated that leaving this richly innervated area intact (Figure 1, ◎) would decrease the incidence of postoperative atrial arrhythmias.

MATERIALS AND METHODS

The impact of fat pad removal at surgery was examined not only in cardio- pulmonary bypass (CPB) procedures but in off-pump coronary artery bypass (OPCAB) procedures as well, where ascending aortic cannulation and atrial manipulation are avoided. In OPCAB procedures, an aortic side biting clamp was placed without disruption of the fat pad.

This was a prospective pilot study of consecutive patients who met criteria for OPCAB at our hospital and who met defined criteria for an atrial arrhythmia (n = 131). One hundred-forty patients were initially entered into the study but 9 were excluded due to pre-existing supraventricular arrhythmias (five) or to peri-operative myocardial infarction (four). Patients were sequentially randomized to either intact or removed fat pad and further assigned to either CPB or OPCAB. We deviated from this in the following unusual circumstances: in a minority of patients the ascending aorta was short and/or calcified and the aortic fat pad extensive, compromising our ability to cannulate and perform the proximal anastomoses. Additionally, on occasion we felt it would be safer for the patient to proceed with CPB rather than an OPCAB, as the coronary vessels were too small and friable, calcified or intromyocardial; or despite the usual maneuvers the patient would not tolerate an OPCAB approach hemodynamically. Patients were assigned to either intact– or removed–fat pad groups and further assigned to either CPB or OPCAB. The number of patients in each group were as follows: CPB/Fat-Pad-Removed, n = 54; CPB/Fat-Pad-Intact, n = 29; OPCAB/Fat-Pad-Removed, n = 19; OPCAB/Fat-Pad-Intact, n = 29.

All patients were monitored with continuous EKG while in the postoperative coronary care unit and by telemetry on the step-down unit and floor until discharged.

Table 1. Selected pre-operative variables

	CPB Fat Pad Removed	CPB Fat Pad Intact	OPCAB Fat Pad Removed	OPCAB Fat Pad Intact
Age (years)	62.7 ± 10.1	61.5 ± 9.0	57.1 ± 9.9	57.8 ± 9.3
Body Mass Index (kg/m^2)	31.5 ± 6.4	28.6 ± 7.6	30.5 ± 3.6	29.8 ± 3.4
Gender (%male)	75.9	88.5	81.2	88.5
Diabetes (% patients with)	40.4	28.6	36.8	24.1
Current Smoker (% smoking)	18.9	17.9	15.8	17.2
History of MI (%with)	32.7	39.3	26.3	24.1
Beta Blockers (% taking)	59.3	65.5	57.9	62.1
Hypercholesterolemia (% with)	80.8	82.1	79	82.8
Calcium Antagonists (% taking)	28.9	28.6	31.6	20.7
Diuretics (% taking)	32.7	14.3	10.5	6.9
Aspirin (% taking)	63.5	82.1	79	89.7
Anti Platelet Meds (% taking)	48.1	67.9	73.7	72.4
STS Predicted Mortality (%)	2.23 ± 1.89[a,b]	1.59 ± 1.29	1.02 ± 0.62[a]	1.09 ± 0.81[b]

[a,b]$P < 0.05$ versus labeled counterpart.

All data were taken by a nurse clinician or physician's assistant. All cases initially reported as atrial arrhythmias were then thoroughly reviewed by a surgeon and nurse to confirm that the patient met the definition of atrial arrhythmia and that no exclusion criteria were present.

One or more of the following specific supraventricular arrhythmias defined an atrial arrhythmia: 1) atrial fibrillation; 2) atrial flutter; or 3) paroxysmal atrial tachycardia. We excluded all transient arrhythmias (arbitrarily determined to last less than 15 minutes and/or occurring only one time) as they were of no clinical importance. Patients with pre-existing supraventricular tachycardia or atrial arrhythmias were excluded from the study as well as patients with peri-operative myocardial infarctions.

In addition to the incidence of atrial arrhythmias, we tabulated or measured: demographics including race, age, sex, height, and weight; all pre-operative medications being taken; risk factors including diabetes, smoking status, ASA and NYHA classifications, STS-predicted mortality, hypercholesterolemia, history of previous myocardial infarction, and congestive heart failure; operative and postoperative factors including the number of distal anastomoses constructed and all complications; and pre-operative and postoperative levels of day-1 electrolytes.

The fat pad was removed in five patients and examined microscopically and by immunohistochemical staining using S100 antibody (Ventana Medical Systems, Inc., Tucson, AZ), which is commonly used in clinical and research applications centering on immunohistochemical documentation of nerve origin. We used a rabbit polyclonal antibody directed against purified S100 protein isolated from a bovine brain. S100 protein is an acidic calcium binding protein comprised of at least two subunits: S100 alpha and S100 beta. A polyclonal antibody recognizes both of these subunits. The protein is known to be expressed in a variety of normal and neoplastic cells. Normal cells known to express S100 include, among others, schwann cells, neurons, and some histiocytes.

Univariate and multivariate logistic regressions (Systat 7.0; SPSS, Inc. Chicago, IL) were employed to determine the importance of all variables in predicting the occurrence of atrial arrhythmias. Chi-square and analysis of variance with Bonferroni tests were used as appropriate to determine similarity of the groups.

RESULTS

We confirmed the presence of neurogenic tissue in the aortic fat pad of humans. Fat pads were removed in five patients. The fat pads ranged from 1.9 to 2.9 cm in maximal dimension. In addition to mature fibroadipose tissue, the fat pads all contained varying numbers of nerve bundles. One pad contained a small caliber nerve of 1.2 cm length. Two pads had focally prominent collections of ganglion cells indicative of parasympathetic innervation.

The groups were similar in all factors (Table 1, ◎) except for the STS predicted mortality which was higher in the CPB/Fat-Pad-Removed group (2.23 ± 1.89) than in either the OPCAB/Fat-Pad-Removed group (1.01 ± 0.62) or the OPCAB/Fat-Pad-Intact group (1.09 ± 0.80); $p < 0.05$ for both comparisons. Stepwise automated multivariate logistic regression was used to determine if any of the variables listed in table 1 were predictive of a poor outcome. The final model showed that only the pre operative medication of calcium antagonists was significant in predicting an atrial arrhythmia (Odds ratio: 4.202, 95% bounds: 1.31 to 13.45, $p = 0.016$).

The data on the incidence of atrial arrhythmias by group are presented in Table 2 (◎). Stepwise automated logistic regression using fat-pad status, pump status, and their cross product as independent variables showed that removal of the fat pad was linked to a higher incidence of atrial arrhythmias (odds ratio = 3.49; 95% bounds: 1.09 to 11.18, $p = 0.035$).

Table 2. Incidence of new-onset atrial arrhythmias.*

	CPB	OPCAB	Total
Fat pad intact	3/29 (10.3)	1/29 (3.5)	4/58 (6.9)
Fat pad removed	11/54 (20.4)	4/19 (21.1)	15/73 (20.5)
Total	14/83 (16.9)	5/48 (10.4)	19/131 (14.5)

*Data are presented as number of arrhythmias/total number of patients per group (percentage).

DISCUSSION

Atrial arrhythmias typically develop during the first few days after surgery with a peak incidence on the second to fourth postoperative day [Creswell 1993]. The mechanism of the initiation of postoperative atrial fibrillation is likely multifactorial. Re-entrant phenomena are one of the primary mechanisms hypothesized [Cox 1991, Cox 1993, Konings 1994]. Extracorporeal circulation, cardioplegic arrest, systemic and cardiac hypotension, atrial manipulation, cannulae placement, and atrial ischemia have all been indicated as contributors to postoperative atrial fibrillation [Johnson 1976, Ormerod 1984, Leitch 1990, McAlister 1990, Caretta 1991, Butler 1993, Middlekauff 1993, Aranki 1996, Yilmaz 1996]. The therapeutic approach therefore is multifaceted. Most treatment approaches are pharmacologic and attempt to lessen the incidence or duration of atrial fibrillation once it occurs. Treatment focuses on control of atrial fibrillation frequency with various pharmacologic agents and cardioversion to achieve a sinus mechanism. A concept of electrical remodeling suggests that, at least in animal models, a longer duration of atrial fibrillation results in cellular alterations that may perpetuate the arrhythmia (i.e., atrial fibrillation begets atrial fibrillation) and increases refractoriness to restoring a sinus mechanism [Wijffels 1995].

The literature is rich with evidence of anatomic and physiologic cardiac innervation in both animals and man [Chiou 1977, Randall 1983, Randall 1985, Burkholder 1992, Armour 1997, Horackova 1999]. Various areas of the heart have been shown to have differing sensitivities to different autonomic inputs. The anatomic pathways are discrete and can be surgically deleted. One anatomic area of such innervation is the aortic fat pad and adjacent aorta and pulmonary artery tissue. Since one of the main hypotheses for postoperative atrial arrhythmias is temporal dispersion of the refractory period leading to re-entrant arrhythmias, any factor contributing to an autonomic imbalance may accentuate a propensity for such arrhythmias. Our data clearly supports this hypothesis.

Studies by Cohn [1999], Puskas [1999] and Bull [2000] suggest that both minimally invasive (MIDCAB) and off-pump multi-vessel coronary artery bypass grafting by a standard median sternotomy result in no decrease in postoperative atrial fibrillation compared with conventional bypass techniques. Conversely, the data of Pompilio et al. [1999] and Arom et al. [2000] suggest that a benefit of OPCAB is reduction of the occurrence of atrial fibrillation.

Our four groups were similar in makeup and studied prospectively. The nurse clinician and physician's assistant were blinded as to the type of surgery performed. There was not absolute randomization. Patients were prepared preoperatively and agreed to an off- or on-pump approach, dependent on clinical findings in the operating room. If the aorta was short and/or calcified, the aortic fat pad extensive, compromising our ability to cannulate when necessary and perform the proximal anastoses or place the partial occluding clamp, the fat pad was then removed. When the coronary vessels were too small and friable, calcified, intramyocardial or, despite usual measures, the patient remained hemodynamically unstable, CPB was initiated rather then the "planned" OPCAB approach. This partially explains the STS predicted mortality differences in the CPB/fat pad removed group, especially in this small pilot study.

In general, leaving the fat pad intact does not limit the area available for cannula (CPB) or graft placement, as grafts may be anastomosed surrounding the fat pad above or below. When space is at a premium, an off-pump approach avoids aortic cannulation or vent placement. Additionally, sequential bypasses, with only one or two proximal anastomoses, may be performed.

Our current data provide a strong suggestion that a synergism effect may be occurring between OPCAB/Fat-Pad-Intact (1 atrial arrhythmia in 29 patients) and CPB/Fat-Pad-Removed groups (11 arrhythmias in 54 patients, $p = 0.128$ by chi-square test). Indeed, this 3.5% incidence versus the 20.4% incidence may be of clinical importance. Avoiding a partial occlusion clamp while performing the proximal aortic anastomosis may further decrease aortic fat-pad manipulation and the incidence of atrial arrhythmias. We plan to study a much larger patient population, with procedures by multiple surgeons, to further validate these results and better define subgroups most influenced by the technique.

CONCLUSION

Retaining the aortic fat pad during cardiac surgery, whether on cardiopulmonary bypass or off pump, markedly decreases postoperative atrial arrhythmias. This should have a major impact in decreasing patient morbidity, length of hospital stay, and cost.

REFERENCES

1. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, et al. Predictors of atrial fibrillation after coronary artery surgery: current trends and impact on hospital resources. Circulation 94:390–7, 1996.
2. Arom KV, Flavin TF, Emery RW, Kshettry VR, Janey PA, Petersen RJ. Safety and efficacy of off-pump coronary artery bypass grafting. Ann Thorac Surg 69:704–10, 2000.
3. Armour JA, Murphy DA, Yuan BX, MacDonald S, Hopkins DA. Gross and microscopic anatomy of the human intrinsic nervous system. Anat Rec 247:289–98, 1997.
4. Burkholder T, Chambers M, Hotmire K, Wurster RD, Moody

S, Randall WC. Gross and microscopic anatomy of vagal innervation of the rat heart. Anat Rec 232(3):444–52, 1992.
5. Bull DA, Stringham JC, Neumayer LA, Karwande SV. CABG with cardiopulmonary bypass versus OPCAB. Does eliminating the pump reduce morbidity and cost? Presented at the36th Annual Meeting of the Society of Thoracic Surgeons, Fort Lauderdale, Florida; Jan–Feb, 2000:108 [Abstract].
6. Butler J, Harriss DR, Sinclair M, Westaby S. Amiodarone prophylaxis for tachycardia after coronary bypass surgery: a randomized double-blind placebo controlled trial. Br Heart J 70: 56–60, 1993.
7. Caretta Q, Mercanti CA, De Nardo D, Chiarotti F, Scibilia G, Reale A, Marino B. Ventricular conduction defects and atrial fibrillation after coronary artery bypass grafting: multivariate analysis of preoperative, intraoperative, and postoperative variables. Eur Heart J 12:1107–11, 1991.
8. Chiuo CW, Eble JN, Zipes DN. Efferent vagal innervation of the canine atria and sinus and atrioventricular nodes. The third fat pad. Circulation 95:2573–84, 1977.
9. Cohn WE, Sirois CA, Johnson RG. Atrial fibrillation after minimally invasive coronary artery bypass grafting: a retrospective, matched study. J Thorac Cardiovasc Surg 117:298–301, 1999.
10. Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C, et al. The surgical treatment of atrial fibrillation. II. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. J Thorac Cardiovasc Surg 101:406–26, 1991.
11. Cox JL. A perspective on postoperative atrial fibrillation in cardiac operations. Ann Thorac Surg 56:405–9, 1993.
12. Cox JL. A perspective on postoperative atrial fibrillation. Semin Thorac Cardiovasc Surg 11:299–302, 1999.
13. Creswell LL, Schuessler RB, Rosenbloom M, Cox, JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg 56: 539–49, 1993.
14. Creswell LL. Postoperative atrial arrhythmias: risk factors and associated adverse outcomes. Semin Thorac Cardiovasc Surg 11:303–7, 1999.
15. Hogue CW, Hyder ML. Atrial fibrillation after cardiac operation: risks, mechanisms, and treatments. Ann Thorac Surg 69:300–6, 2000.
16. Horackova M, Armour JA, Byczko Z. Distribution of intrinsic cardiac neurons in whole-mount guinea pig atria identified by multiple neurochemical coding. A confocal microscope study. Cell Tissue Res 297:409–21, 1999.
17. Johnson LW, Dickstein RA, Fruehan CT, Kane P, Potts JL, Smulyan H, et al. Prophylactic digitalization for coronary artery bypass surgery. Circulation 53:819–22, 1976.
18. Konings KT, Kirchhof CJ, Smeets JR, Wellens HJ, Penn OC, Allessie MA. High-density mapping of electrically induced atrial fibrillationin humans. Circulation 89:1665–80, 1994.
19. Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. J Thorac Cardiovasc Surg 100:338–42, 1990.
20. McAlister HF, Luke RA, Whitlock RM, Smith WM. Intravenous amiodarone bolus versus oral quinidine for atrial flutter and fibrillation ater cardiac operations. J Thorac Cardiovasc Surg 99:911–8, 1990.
21. Middlekauff HR, Wiener I, Stevenson WG. Low-dose amiodarone for atrial fibrillation. Am J Cardiol 72:75F–81F, 1993.
22. Ormerod OJM, McGregor CGA, Stone DL, Wisbey C, Petch MC. Arrhythmias after coronary bypass surgery. Br Heart J 51:618–21, 1984.
23. Pompilio G, Antona C, Cannata A, Lotto A, Alamanni F, Gelpi G, et al. Coronary surgery without extracorporeal circulation: the short-term results in high-risk patients. G Ital Cardiol 29:246–54, 1999.
24. Puskas JD, Wright CE, Ronson RS, Brown WM, Gott JP, Guyton RA. Clinical outcomes and angiographic patency in 125 consecutive off-pump coronary bypass patients. The Heart Surgery Forum #1999-95310 2:216–21, 1999.
25. Randall WC, Thomas JX, Barber MJ, Rinkema LE. Selective denervation of the heart. Am J Physiol 244:H607–13, 1983.
26. Randall WC, Ardell JL. Selective parasympathectomy of automatic and conductile tissues of the canine heart. Am J. Physiol 248(1 pt 2):H61–8, 1985.
27. Wijffels MC, Kirchhof CJ, Dorland R, Allessie MA. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. Circulation 92:1954–68, 1995.
28. Yilmaz AT, Demirklilic U, Arslan M, Kurulay E, Ozal E, Tatar H, Oxturk O. Long-term prevention of atrial fibrillation after coronary artery bypass surgery: comparisons of quinidine, verapamil and amiodarone in maintaining sinus rhythm. J Cardiac Surg 11:61–4, 1996.