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Coronary Artery Bypass Surgery for Patients Presenting with Ventricular Arrhythmias: Propensity Matched Early and Late Outcome

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Abstract

Objectives: Patients with ischemic ventricular arrhythmia (IVA) in the form of fibrillation or tachycardia represent a surgical challenge. Evidence in the literature suggests that ventricular arrhythmia threatens survival even after cardiac surgery. We aim to review the results of our patients presenting with IVA with regard to short and long term outcome following cardiac surgery. Methods: This was a retrospective study of data entered prospectively into our cardiac surgical database between January 1999 and September 2015. A total of 9609 patients underwent Cardiac Surgery which included 54 patients after surviving IVA. The short- and long-term outcomes were compared to a propensity matched group. Actuarial survival was calculated using Kaplan Meier analysis. Results: The 54 study group patients were propensity matched on a 1:2 basis with a control group of non-IVA (n = 108). The baseline preoperative characteristics and risk factors were similar between the 2 groups and all cases underwent CABG only. Univariate analysis showed pacing postoperatively (33.3 vs 66.7%; p = 0.001) and postoperative ventricular arrhythmia (10 vs 22.2%; p = 0.039) to be significantly higher in the IVA group. Cox-multivariate analysis showed postoperative ventricular arrhythmia in either group (Hazard ratio = 1.5) to be the only significant factor to impact mortality (p < 0.001). Long term survival was not significantly different between the two groups (10.4; CI: 9.08 - 11.75 vs 9.3; CI: 7.61 - 11.01 yrs, p = 0.3). Conclusion: Cardiac surgery on patients presenting with IVA can be performed safely yielding short and long term results equivalent to non-IVA cases. These patients should not be denied surgery with consideration of good long term outcome.

Keywords

Ischemic Ventricular Arrhythmia (IVA), Ventricular Fibrillation (VF), Implantable Cardioverter (ICD), Coronary Artery Disease (CAD)

1. Introduction

Arrhythmias and ischemic heart disease comprise a significant percentage of sudden cardiac death especially in the older population [1] [2]. Patients with ischemic heart disease presenting with ventricular arrhythmias (VA) represent a high risk population compared to the rest of the patients undergoing surgical revascularisation [3]. Randomised control trial on this subgroup of patients is not feasible due to ethical and clinical restraints and although a number of studies assessed short and long term outcomes of these ischemic patients presenting with VAs none seems to have a proper control group [4] [5] [6]. The absence of a control group raises concerns over any conclusions. In this study we aim to assess the short and long term outcomes of patients undergoing surgical revascularisation following presentation with VA against an equivalent control group by propensity matching. Propensity matching empowers the retrospective study. It allows comparable results and conclusions to those of a randomised controlled study [7].

Given the increased incidence of annual VA (8%) even after revascularisation [8], we also reviewed the impact of completeness of revascularisation and ICD insertion on these outcomes in our data.

2. Methods

2.1. Design

This is a retrospective study of all patients that underwent coronary artery bypass surgery (CABG) between January 1999 and September 2015 and included in our database at Hull and East Yorkshire Hospitals NHS Trust was examined. We identified a total of 9609 patients who underwent CABG with 54 (5.62%) of them having survived an ischemic ventricular arrhythmia (IVA). Operative mortality was defined as occurring during the operative hospitalization or within 30 days of operation for discharged patients. The preoperative characteristics were as defined by the EuroSCORE I criteria [9].

Other secondary outcomes were: Perioperative intra-aortic balloon pump, sternal resuturing, postoperative myocardial infarction, postoperative arrhythmias and permanent pacing, pulmonary complications, wound infections, gastrointestinal complications and multiorgan failure.

2.2. Propensity Score Matching

Using "R" program [10]; patient's preoperative characteristics (Age, gender, BMI), comorbidities (neurologic, renal, pulmonary), Ejection fraction, urgency of operation and logistic EuroSCORE were used to develop a score (propensity score) for each case. The 54 post IVA patients were propensity matched to patients that underwent CABG without prior IVA in a 1:2 ratio (n = 108).

Individual informed consent was waived due to the fact that the data was already available for clinical and research purposes. Furthermore, the data was in a format that would not allow any individual patient to be identified (anonymised).

2.3. Statistical Analysis

1) Univariate analysis:

Categorical data are summarized using percentages. Continuous data are presented as the mean value (±standard deviation). Categorical data were compared by Chi-squared test. Continuous data were tested against "Normal" Plot and "Q-Q" plots; those of normal distribution were compared using student t-test while non-normal distributed data were compared by "Mann-Whitney test".

2) Multivariate analysis:

Cox multivariate analysis was used to identify the impact of the significant factors from the univariate analysis on the long term survival.

2.4. Long Term Survival

Long term survival for each group was analysed using Kaplan-Meier curves and then compared by the log rank test to calculate the p-value.

A p-value of <0.05 was considered statistically significant. The 95% confidence interval is calculated according to Brookmeyer & Crowley.

Statistical analyses were performed using MedCalc for Windows, version 13.1.2 (MedCalc Software, Ostend, Belgium).

3. Results

Baseline criteria:

The baseline criteria for all the cases that underwent cardiac surgery in our unit are shown in **Table 1**.

Study flow chart:

The flow chart (**Figure 1**) shows how the study and the control groups were obtained and their relevant sizes.

Propensity scoring and matching:

Using R computer programming each patient from the patient population was given a score depending on the factors mentioned in the methods section. Based on the score, each patient from the study group was matched with the closest two patients from the control group (**Figure 2**).

Univariate analysis:

Analysis of the pre-, intra- and postoperative factors identified post operative VF and permanent pacemaker insertion were significantly higher in the study group (**Table 2**).

Table 1. Baseline criteria for the database (n = 9609). Absolute numbers (percentage of total) or mean ± standard deviation (SD).

Preoperative criteria	
Age	65.8 ± 10.2
Gender (male)	6939 (72.2%)
NYHA class (4)	369 (3.8%)
CCS class (4)	995 (10.4%)
Hypertensive	7248 (75.4%)
Diabetic	1705 (17.7%)
Ex/current smoker	6148 (64.0%)
Patients on long term inhalers	1163 (12.1%)
Preoperative renal dysfunction	217 (2.3%)
Neurologic dysfunction	95 (1.0%)
Peripheral vascular disease	952 (9.9%)
Preoperative inotropic support	87 (0.9%)
Preoperative nitrate infusion	532 (5.5%)
Preoperative ventilation	48 (0.5%)
Preoperative cardiogenic shock	65 (0.7%)
Preoperative MI	3174 (33.0%)
Left ventricular ejection fraction (Poor)	565 (5.9%)
Preoperative VF/VT	54 (0.6%)
Redo sternotomy	556 (5.8%)
BMI	28.1 ± 4.5
Logistic EuroSCORE	5.3 ± 8
Operative Criteria	
Urgency (emergency)	193 (2%)
Perioperative IABP	93 (1.0%)
Not isolated CABG	3144 (32.7%)
Off bypass CABG	469 (4.9%)
Perfusion time	71.2 ± 34.7
Cross clamp time (min)	41.9 ± 22.8
Post operative criteria	
Average hospital stay (days)	9.4 ± 11.1
Postoperative permanent stroke	100 (1.0%)
low cardiac output (requiring inotropes, IABP or VAD)	3081(32.1%)
Re-exploration	416 (4.3%)
ITU readmission	367 (3.8%)
New postoperative dialysis	152 (1.6%)
In-hospital mortality and 30 day mortality	307 (3.2%)

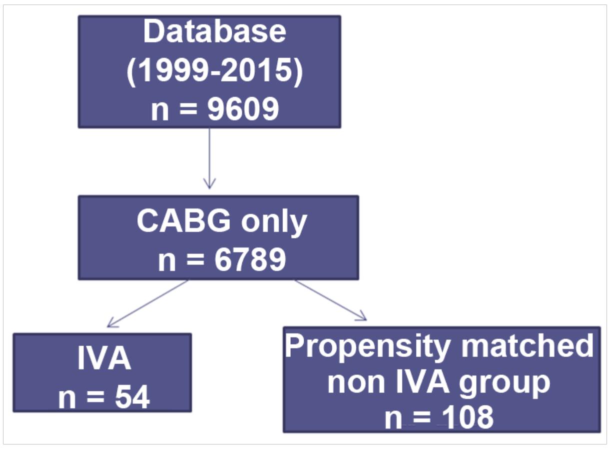


Figure 1. Flow chart showing the control and study groups.

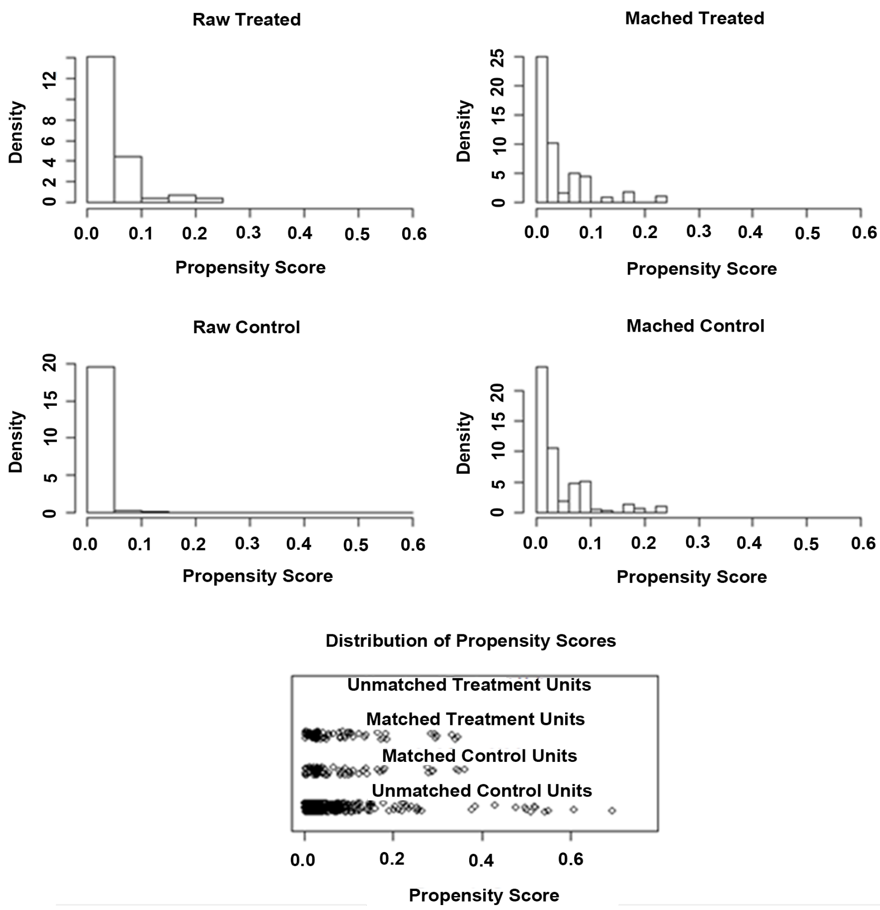


Figure 2. Bar charts and dot graph showing the propensity matched control and study groups.

Cox multivariate analysis (predictors of long term survival):

Multivariate analysis revealed that the only factor impacting on in hospital mortality was postoperative VF (HR 1.5) as seen in **Table 2**.

Significantly higher in the study group. Multivariate analysis showing Post-operative VF the only factor impacting on in-hospital mortality.

Table 2. Univariate analysis showing postoperative VF and permanent pacing were significantly higher in the study group. Multivariate analysis showing Postoperative VF the only factor impacting on in-hospital mortality.

Variable	Study group (IVA n = 54)	Control group (Non IVA n = 108)	p value
Age (Mean)	67.1852	68.2963	0.454
Gender (M)	81.5%	67.6%	0.064
NYHA IV	9.3%	10.2%	0.330
Previous MI	66.7%	68.5%	0.815
Preoperative unstable angina (within 31 d)	1.9%	0	0.157
Previous operation	7.4%	6.5%	0.557
Diabetes	24.1%	33.3	0.228
Hypertension	77.8	63	0.058
Preoperative GI morbidity	18.5	14.8%	0.546
Preoperative inotropes	1.9	0	0.157
Preoperative nitrates/heparin	20.4	29.6	0.210
Preoperative congestive HF	37%	26.9%	0.185
Cardiogenic shock	0	1.9	0.316
Preoperative ventilation	1.9	0.9	0.616
Logistic EuroSCORE	13.1	10.68	0.188
CPB	94.4%	88.9%	0.252
X clamp time (mean-min)	27.5	27.9	0.860
Bypass (mean-min)	58	60.2	0.664
Reopening for bleeding	3.7	4.6	0.785
Low COP	66.7	56.5	0.214
ITU recidivism	3.7	4.6	0.785
Renal complication	0	2.8%	0.218
Neurologic complication	0	0.9	0.480
Post op stay (d)	10.5	10.13	0.851
No. Of diseased vessels	2.57	2.7	0.253
LMS	41.7%	42.6%	0.911
Distal anastomoses	2.54	2.58	0.694
Perioperative IABP	5.6	13	0.148
Sternal resuturing	1.9%	1.9%	1.000
Perioperative Q wave	0	0.9%	0.480
Postoperative MI	0	3.7%	0.153
Postoperative Arrhythmia (VF)	22.2%	10.2%	0.039
Postoperative AF	25.9%	31.5%	0.467
Postoperative PPM	66.7%	28.4%	0.001
Pulmonary complications	22.2%	23.1%	0.895
Postoperative GI complications	5.6%	6.5%	0.818
Multi organ failure	0%	2.8%	0.218
In-hospital mortality	3.7%	10.2%	0.154
Cox proportional-hazards regression			
Variable	Hazard Ratio	95% CI	p value
Postoperative Arrhythmia (VF)	1.524	1.268 to 1.832	<0.001

Long term survival:

Kaplan Meier analysis of the long term survival at 15 years postoperatively showed 7/108 (control group) versus 6/54 (study group) alive. The median survival was 13 (control group) and 10 years (study group). This was not significant by log rank test (p = 0.33) as demonstrated in **Figure 3**.

Subgroup analysis of Patients with persistent VA in the study group:

12 (22.2%) patients in the IVA group had postoperative VF. 2 died in hospital (No EPS performed). 5/10 discharged patients had ICDs inserted (Mean 5.86 years survival). 3/10 discharged did not require ICD (Mean 5.66 years survival). 2/10 needed PPM (Mean 2.85 years survival). The relation between ICD/PPM insertion and LV function (in patients that had postoperative VF and were discharged home alive) is shown in **Table 3**.

The ratio between the extent of coronary artery disease to number of bypass grafts was as follows:

Preoperative sinus rhythm and postoperative non-VA: 0.95, preoperative sinus rhythm and postoperative VA: 1.03, preoperative IVA and postoperative non-VA: 0.99 and preoperative IVA with postoperative IVA: 0.97.

4. Discussion

VAs are a fatal complication of ischemic heart disease. Many earlier studies claimed better short [3] [11] and long term survival following revascularisation [12]. However, these studies failed to compare this outcome with an "equivalent" control group with *suboptimal deduction of conclusions*.

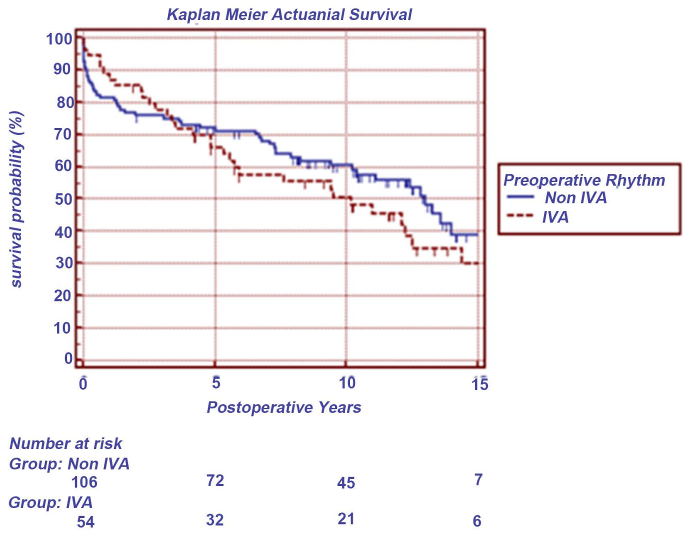
The difference in the preoperative characteristics between the database and the propensity matched control group highlights the relevance of performing propensity matching, allowing comparison between homogenous groups, not only performing a similar operative procedure, but with similar characteristics.

To the best of our knowledge, this is the first study to compare the short and long term outcomes following surgical revascularisation with a similar population, risk profile-wise; by propensity scoring and matching. We shall base our discussion on the following questions:

1) Ischemic patients with preoperative VA have up to 8% annual recurrence of their VA (MADT-CRT) [11] even following there revascularisation. Should this fact impact on conduit choice and completion of grafting (e.g., arterial revascularisation)?

2) With such a high risk profile, rapid surgical revascularisation of the culprit lesions; as performed in primary PCI, should suffice and allow these high risk patients to be discharged home from a quick operation rather than end up with prolonged ITU stay and in-hospital mortality while the remaining CAD may be dealt with by hybrid PCI?

The two groups had similar short term outcomes (except for a higher incidence of postoperative VA and pacemaker insertion). There hospital stay was similar (9 days) which was either due to prolonged ITU stay (from Inotropic, IABP, respiratory and renal causes) and ward stay (due to wound break down



Factor	95% CI for the mean	Median	95% CI for the median
Control group	9.08 to 11.75	12.98	10.20 to 13.98
Study group	7.61 to 11.01	10.17	5.54 to 14.37
Comparison of survival curves (Log rank test)			
Significance	P = 0.33		

Figure 3. Kaplan Meier curves for the control and the study groups showing no significant difference in the long term survival.

Table 3. Relation between postoperative VF (in the IVA group) and LV function.

Discharged IVA patients that had postoperative VF	Good LV	Fair LV	Poor LV
3 no PPM	1	1	1
5 ICD	1	1	3
2 VVI/DDD	0	1	1

and infection). Both groups had complete revascularisation (Table 2). In hospital mortality for both groups was statistically similar (p = 0.15). Hence; *prolonged bypass and cross clamp time for the sake of adequate revascularisation* has not impacted negatively on the short term outcomes.

Long term survival was similar between the control and study group (p = 0.33). From the significant factors on univariate analysis, only persistent postoperative VA significantly affected long term survival (HR 1.5) in the multivariate analysis. Causes of postoperative VA are multiple and interrelated: electrolyte disturbance, poor perfusion secondary to low cardiac output, inadequate revascularisation, arrhythmogenic inotropes and even genetic [11]. It is difficult to diagnose the exact cause in most cases and some of these causes are unavoidable, such as genetic predisposition. The most important avoidable factor in theatres is inadequate revascularisation which we investigated in more detail by comparing the number of ischemic vessels with the number of grafts in the various subgroups (Table 2 and the last paragraph in the results section) and have not found any difference between the patients that had postoperative VA from the study and control groups as compared to those that had no postoperative VA in both groups. Hence we again conclude that complete revascularisation and choice of conduits should not be jeopardised as patients with preoperative VA have a similar long term survival equivalent to high risk non VA patients. Other studies have suggested the relevance of surgical revascularisation over ICD insertion [13].

All patients that needed postoperative ICD had impaired LV but one. The patient with a good LV underwent ICD insertion 1 month postoperatively based on electrophysiologic studies performed preoperatively. This was prior to the recommendations of MADIT-CRT and SOLVD in 2006 [11] [13]-[18], which stated that the benefits of ICD insertion are after 6 months and a significant proportion of patients, especially those with preserved LV, will remodel and avoid the need for an ICD during this period. Also the mean survival of patients with postoperative VF in the study group that needed an ICD (5.86 years) was similar to those that did not need an ICD (5.66 years). This highlights that even with persistent aetiologies of post operative VA that cannot be reversed, long term survival may be preserved with ICD insertion [12]. The 2 patients that needed postoperative pacing had a shorter mean survival (2.85 years). We could not identify the reason for this and the causes of death could not be identified weather cardiac or non cardiac.

Strengths & Limitations

Propensity scoring and matching allowed us to compare the effect of treatment (surgical revascularisation) on observational data. The advantage of using a linear combination of covariates for a single score allows balancing a test group with a control group without losing a large number of observations (cases). In our case the "pool" of data allowed a "greedy" match for the chosen confounding variables.

One disadvantage is that the matching is only for the chosen variables and the rest of the risk factors and comorbidities remain unmatched. Nevertheless, PSM has been assessed by other studies to validate the effect of treatment on observational data [7] [19] [20].

The intrinsic limitations of selection bias are inherent to all observational data. Also, failure to attain the cause related mortalities in long term studies is a common drawback for long term studies.

5. Conclusions

1) Coronary Artery Bypass surgery on patients presenting with IVA can be performed safely yielding short and long term results equivalent to non-IVA

cases.

2) Persistence of Postoperative Ventricular Fibrillation is the single predictor for long term mortality in this population.

3) Cardiology referral to assess the need for ICD insertion is essential post-operatively.

These patients should not be denied surgery with consideration of good long term outcome.

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Conflicts of Interest Statement

There is no conflict of interest to declare.

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