

**ROLE OF INTRAOPERATIVE POSTERIOR PERICARDIAL WINDOW
IN PREVENTING POSTOPERATIVE ATRIAL FIBRILLATION
IN ON-PUMP CORONARY ARTERY BYPASS GRAFTING PATIENTS**



Thesis Submitted By

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*In Partial Fulfillment of the Requirement
for the Award Of*

**Post Doctoral Fellowship
in
Adult Cardiac Surgery 2021**

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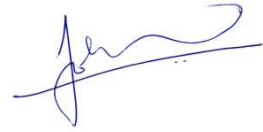
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DECLARATION

I, Dr. JOHN MATHEW K, hereby declare that this thesis titled ***“Role of Intraoperative Posterior Pericardial Window in Preventing Postoperative Atrial Fibrillation in On-Pump Coronary Artery Bypass Grafting Patients”*** has been prepared by me under the supervision and guidance of Dr.VIVEK V. PILLAI, Professor, Department of CVTS and Dr.RENJITH S, Assistant Professor, Department of CVTS, Department of Cardiovascular and Thoracic Surgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram, Kerala, India-695011



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CERTIFICATE

We hereby certify that this thesis titled **ROLE OF INTRAOPERATIVE POSTERIOR PERICARDIAL WINDOW IN PREVENTING POSTOPERATIVE ATRIAL FIBRILLATION IN ON-PUMP CORONARY ARTERY BYPASS GRAFTING PATIENTS** is the bonafide work of Dr. John Mathew K, Post Doctoral Fellow (Adult Cardiac Surgery), done under our guidance at Department of Cardiovascular and Thoracic Surgery at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram, Kerala, India.

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Dr . Baiju S Dharan

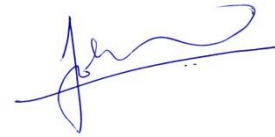
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ACKNOWLEDGEMENT

Writing this thesis had been difficult but extremely rewarding. I would like to thank a number of people who have contributed to the final result in many different ways.

An ostentatious use of words will not be sufficient to express my heartiest thanks to my guide Dr.Vivek V. Pillai, Professor, and co-guide Dr.Renjith S, Assistant Professor, Department of Cardiovascular and Thoracic Surgery. Their valuable and critical suggestions, constant inspiration and encouragement, instinctive corrective measures, timeless efforts, unstinted cooperation and mental support throughout have made this herculian task a smooth journey.

I will always remain obliged and grateful to my head of the department, Professor Dr. Baiju S. Dharan for his invaluable support.I have to mention gratitude to my Consultants Dr. Varghese T Panicker, Dr.Bineesh K. Radhakrishnan, Dr. Simon Philipose, who have been instrumental and constantly supported me during the course.

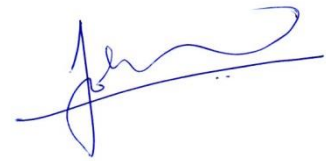
I would like to express my gratitude to all Senior Residents of the department for their support throughout.

Sincere thanks to all other staff of department of Cardiovascular and Thoracic surgery for their understanding, inspiration and affectionate encouragement right from the start of this course and work.

Sometimes it is not easy to express in words especially when you have to say thanks to your parents for their constant undemanding love, dedication, sacrifice, inspiring guidance, affectionate encouragement and never ending enthusiasm, without which this study would not have seen the light of the day. Thanks to my parents Mr.

Santhosh K. John and Mrs. Lizy Cherian, my beloved wife Dr. Lydia James George and my sister, Miss. Deena Susan Mathew for their constant encouragement and support while doing the Fellowship programme. I would like to express my gratitude to all my teachers and friends who have been instrumental in all my achievements. I express my sincere gratitude to Dr. Oommen P Mathew, Research Investigator, Population Research Centre, University of Kerala, Thiruvananthapuram for helping me out with the statistical analysis.

Last, but not the least, I thank the Almighty God for being the silent force behind everything.



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LIST OF ABBREVIATIONS

AF	:	Atrial Fibrillation
CABG	:	Coronary Artery Bypass Grafting
CI	:	Confidence Interval
ECG	:	Electrocardiogram
ERP	:	Effective Refractory Period
g/dL	:	Gram per deciliter
Hb	:	Hemoglobin
ICU	:	Intensive Care Unit
IL2	:	Interleukin 2
IL6	:	Interleukin 6
ITT	:	Intention to treat
LA	:	Left Arterial
LVEF	:	Left ventricular Ejection Fraction
OR	:	Odd's Ratio
p	:	p- value
POAF	:	Postoperative Atrial Fibrillation
RA	:	Right Arterial
RCT	:	Randomized Controlled Trial
ROS	:	Reactive Oxygen Species

Abstract

Objectives: To check whether the creation of left posterior pericardial window during on-pump coronary artery bypass grafting surgery shows better results in terms of occurrence of post operative atrial fibrillation when compared to conventional surgery without creation of left posterior pericardial window

Methods:

Data of patients who underwent isolated coronary artery bypass grafting for stable ischemic heart disease was analysed retrospectively. The primary outcome noted was prevalence of postoperative atrial fibrillation in seven days post surgery in patients who had pericardial window and those who didn't have, with separate check of on-pump and off-pump CABG cases.

Results:

Mean age of the patients who had pericardial window created was 59.3 ± 9.4 years and 58.6 ± 9.5 years in on-pump and off-pump CABG cases respectively. Out of 495 patients who underwent on-pump CABG, 434 patients were males (87.6%) and 61 were females (12.3%). Among 22 patients who underwent off-pump CABG, 19 were males (86.3%) and 3 were females (13.6%). In on-pump CABG cases, number of patients in which pericardial window was created was 200 (40.4%) and patients who developed AF after pericardial window creation was 27 (13.5%) as against 63 (21.4%) in patients who developed AF without pericardial window creation. POAF was found to be significantly lower in the pericardial window group than no-pericardial window group undergoing on-pump CABG ($\chi^2 = 4.94$, $p = 0.026$). This difference was not seen in off-pump CABG group. There was no mortality difference between the pericardial and no-pericardial window group for both on-pump and off-pump CABG. Duration of hospital stay in pericardial window group (on-pump CABG) was smaller (mean: 6.9 days) than no-pericardial window group (mean: 7.3

days) but was not statistically significant. However in patients with pericardial window who developed AF, in duration of post operative hospital stay was significantly higher (mean : 8.9 days) than those who didn't develop AF (mean : 6.6 days); $t=2.45$, $p=0.015$.

Conclusions:

Posterior pericardial window creation is safe and simple technique that significantly reduces the prevalence of POAF should be routinely employed in cardiac surgery units.

INTRODUCTION AND BACKGROUND

Post-operative atrial fibrillation (POAF) is one of the commonest complications of cardiac surgery which have significant effects in the morbidity as well as mortality of patients. Preexisting atrial enlargement, as well as markedly elevated sympathetic outflow, intense inflammation, and oxidative stress caused by cardiac surgery, are widely believed to be the major predisposing factors to POAF.⁵⁻⁷

POAF is a clinically important complication of CABG surgery and valvular surgery and has characteristic features. The prevalence of POAF reported in different studies ranges between 20% and 40% reflecting differences in AF definitions, monitoring and screening.⁸⁻⁹ AF after cardiac surgery is typified by episodes that are often brief, paroxysmal and asymptomatic.

POAF after cardiac surgery is associated with increased short-term^{14, 17-19} and long-term morbidity and mortality, including an eightfold increase in the risk of subsequent AF¹³, as well as a higher rate of stroke¹³ and cardiovascular death^{13, 15,16}. The high long-term AF recurrence rate raises questions about the totally transient nature of POAF and points to an interaction between transient perioperative factors and a pre-existing substrate. The AF recurrence rate in patients who develop POAF after cardiothoracic surgery (46%) is lower than that in patients with POAF after non-thoracic surgery (64%)²⁰, supporting a greater role of transient factors than of a pre-existing substrate. Moreover, the long-term risk of stroke is lower with POAF complicating cardiac surgery than with POAF complicating non-cardiothoracic surgery.²¹ The high AF recurrence rates in patients with POAF make this condition a clear marker of subsequent risk of AF.

After CABG operation, the space anterior to the heart can be easily drained by placing a chest drain underneath the sternum, whereas the posterior one is a closed space behind the heart that cannot be easily drained with a chest drain placed underneath the heart that can cause mechanical irritation in addition to its close proximity to the grafts. The idea of opening this dead space posterior to the heart into the left pleural space by creating posterior pericardial window was proved by many studies¹⁻⁴ to drain freely into the pleural space reducing the prevalence of

pericardial effusion and AF. Posterior pericardiotomy is a procedure designed to prevent postoperative pericarditis, in which an incision is made to the posterior pericardium, connecting the pericardial space to the left pleural space but preserving the major neural inputs to the heart.



REVIEW OF LITERATURE

In a recent study published in *The Lancet*, Gaudino et al.²⁴ did a randomised, controlled trial, where they recruited adult patients (aged ≥ 18 years) undergoing elective interventions on the coronary arteries, aortic valve, or ascending aorta, or a combination of these, performed by members of the Department of Cardiothoracic Surgery from Weill Cornell Medicine at the New York Presbyterian Hospital in New York, NY, USA. Patients were eligible if they had no history of atrial fibrillation or other arrhythmias or contraindications to the experimental intervention. Eligible patients were randomly assigned (1:1), stratified by CHA₂DS₂-VASc score and using a mixed-block randomisation approach (block sizes of 4, 6, and 8), to posterior left pericardiotomy or no intervention. Patients and assessors were blinded to treatment assignment. Patients were followed up until 30 days after hospital discharge. The primary outcome was the incidence of atrial fibrillation during postoperative in-hospital stay, which was assessed in the intention-to-treat (ITT) population. Safety was assessed in the as-treated population.

Between Sept 18, 2017, and Aug 2, 2021, 3601 patients were screened and 420 were included and randomly assigned to the posterior left pericardiotomy group (n=212) or the no intervention group (n=208; ITT population). The median age was 61.0 years (IQR 53.0–70.0), 102 (24%) patients were female, and 318 (76%) were male, with a median CHA₂DS₂-VASc score of 2.0 (IQR 1.0–3.0). The two groups were balanced with respect to clinical and surgical characteristics. No patients were lost to follow-up and data completeness was 100%. Three patients in the posterior left pericardiotomy group did not receive the intervention. In the ITT population, the incidence of postoperative atrial fibrillation was significantly lower in the posterior left pericardiotomy group than in the no intervention group (37 [17%] of 212 vs 66 [32%] of 208 [$p=0.0007$]; odds ratio adjusted for the stratification variable 0.44 [95% CI 0.27–0.70; $p=0.0005$]). Two (1%) of 209 patients in the posterior left pericardiotomy group and one (<1%) of 211 in the no intervention group died within 30 days after hospital discharge. The incidence of post operative pericardial effusion was lower in the posterior left pericardiotomy group than in the no intervention group (26 [12%] of 209 vs 45 [21%] of 211; relative risk 0.58 [95% CI 0.37-0.91]). Post

operative major adverse events occurred in six (3%) patients in the posterior left pericardiotomy group and in four (2%) in the no intervention group. No posterior left pericardiotomy related complications were seen. The study concluded that posterior left pericardiotomy is highly effective in reducing the incidence of atrial fibrillation after surgery on the coronary arteries, aortic valve, or ascending aorta, or a combination of these without additional risk of postoperative complications.

In a systematic review and metaanalysis by Xiong et al.¹²⁷, ten RCTs with 1829 patients (910 in the pericardial window group and 919 in the control group) were included in the meta-analysis. The incidence of AF was 10.3% (94/910) in the pericardial window group and 25.7% (236/919) in the control group. A random-effects model indicated that incidence of AF after CABG was significantly lower in the pericardial window group than in the control group (risk ratio=0.45, 95% confidence interval 0.29–0.64, $P < 0.0001$). The study concluded that pericardial window may be a safe, effective, and economical method for preventing AF after CABG in adult patients.

In a multicentre randomized prospective study by Fawzy et al.¹⁰, the posterior pericardiotomy significantly reduced POAF ($P = 0.01$). Similarly, Farsak et al.¹ and Kuralay et al.³ also reported significantly lower incidence of AF in the posterior pericardiotomy group. In contrast, Arbatly et al.⁴ and Asimakopoulos et al.¹¹ demonstrated that posterior pericardiotomy was more effective in draining the pericardial effusion, but the incidence of POAF was not significantly reduced compared with their control group (20 vs 26%). Posterior pericardiotomy is not without complication as Yorgancioglu et al.¹² experienced a problem of haemodynamic instability and uncontrollable arrhythmias due to protrusion of a sequential graft through the posterior pericardiotomy opening.

A metaanalysis of 12 small trials with significant heterogeneity ($I^2 > 50\%$) found that posterior pericardiotomy decreased the incidence of post-cardiac surgery pericardial effusions (OR 0.04, 95% CI 0.02–0.08) and tamponade (OR 0.07, 95% CI 0.02–0.27) at the expense of an increase in the number of pleural effusions (OR 1.64, 95% CI 1.23–2.20)²². In a meta-analysis of ten studies, posterior pericardiotomy reduced the incidence of POAF (OR 0.36, 95% CI 0.23–0.56), albeit with significant interstudy

heterogeneity ($I^2=55\%$)²³.

Lacunae in Literature:

At present, insufficient evidence is available to support the benefit of posterior pericardiotomy, particularly in the context of optimal prophylaxis with β -blockers. So it is worthwhile to look into the effects of this small technique in detail which is deemed relatively safe as per the available knowledge. There have been very little large scale studies related to the subject worldwide and almost nil from India.

RESEARCH QUESTION

Does the creation of left posterior pericardial window during coronary artery bypass grafting surgery reduces the occurrence of post operative atrial fibrillation?



AIMS AND OBJECTIVES

Aim of this study is to compare the outcome following coronary artery bypass grafting surgery with and without intraoperative creation of left posterior pericardial window, in terms of occurrence of post operative atrial fibrillation.

Objective of this study is to check whether the creation of left posterior pericardial window during coronary artery bypass grafting surgery shows better results in terms of occurrence of post operative atrial fibrillation when compared to conventional surgery without creation of left posterior pericardial window.

MATERIALS AND METHODS

(1) Subject/Participant Selection:

(a) **Type:** Patients who underwent elective isolated Coronary Artery Bypass Grafting surgery for Stable Ischemic Heart Disease (Coronary Artery Disease) with and without intraoperative creation of posterior pericardial window, in SCTIMST, Thiruvananthapuram.

(b) **Number:** (i) Total number: 517 patients.(ii) Rational for having that number or sample size : Includes all patients who underwent coronary artery bypass grafting with intraoperative posterior pericardial window creation since its inception in the department. (iii) Sampling method: To include all patients till date fulfilling the inclusion criteria (iv) What proportion of them will be women: Proportion of women will depend upon number of female patients who underwent elective CABG, essentially without any bias toward the gender selection criteria. (v) From where they will be recruited: Patients who underwent elective CABG (with and without posterior pericardial window creation) in SCTIMST. (vi) Whether screening of larger number will be required: No.

(c) Eligibility:

Inclusion criteria: Males and females upto the age of 75 years who underwent isolated elective on-pump CABG surgery for stable ischemic heart disease(coronary artery disease) with and without creation of posterior pericardial window, who had left ventricular function(LVEF) >30% and no preoperative cardiac arrhythmias.

Exclusion criteria: Patients with

- 1) Age more than 75 years
- 2) Severe left ventricular dysfunction (LVEF<30%)
- 3) Preoperative cardiac arrhythmias
- 4) Redo/emergency CABG
- 5) Combined procedures(eg.,valve procedure + CABG)
- 6) Congenital heart diseases

- 7) Need to go on cardiopulmonary bypass again after coming off once during the surgery

Analysis of off-pump CABG cases will be done separately.

(d) **Recruitment** : Patients who underwent elective CABG procedure with and without posterior pericardial window creation was recruited for study by the investigating surgeon (Principal Investigator), considering the inclusion and exclusion criteria, from the hospital medical records, after obtaining due permission from the concerned authority (as per SCTIMST norms).

(2) Data Collection Procedures:

Proposed study protocol & conduct of study:

It is a retrospective study aimed to be conducted with details obtained from the hospital medical records of the patient (operating room register, operation record, cardiac surgical intensive care unit monitoring charts and post-operative ward monitoring charts).

As per the department protocol, all patients are monitored continuously with electrocardiogram (ECG) in the operating room during the procedure and in the cardiac surgical intensive care unit post procedure. After getting shifted to ward, they are monitored with 12-lead ECG when clinically indicated and before discharge. The required data for the study is hence available in the medical records.

The **primary outcome** will be prevalence of postoperative atrial fibrillation in 7 days post surgery.

Other relevant preoperative, operative and postoperative data will be collected from computerized hospital information system and cardiac surgical ICU & ward monitoring charts. All parameters will be collected as per the data collection form designed for the study and based upon the methods of data collection.

Method of Randomisation and Blinding:

No randomisation is employed in the study. All patients who meet the inclusion criteria, operated till date will be analysed in the study.

During CABG, after grafting of lateral wall coronary artery (OM-obtuse marginal branch), a posterior vertical left pericardiotomy of approximate length 3-4cm and width 1-2cm is created posterior and parallel to left phrenic nerve resulting in the creation of posterior pericardial window. Intraoperative monitoring of ECG is continued from the operating room to cardiac surgical ICU to detect any development of atrial fibrillation. After patient is shifted to ward following stabilization of hemodynamics, ECG will be taken to check the rate and rhythm of the patient if clinically indicated to detect atrial fibrillation if any.

Treatment:

If the patient developed atrial fibrillation, the chain of events and treatment given as per department protocol would have been documented and can be retrieved from medical records.

Interviews, Discussions, Observations:

As this is a retrospective study, no interviews or discussions are held (with patients). Observations are recorded in the study proforma.

Follow up:

No follow up is done.

Specific locations where they will be performed and by whom:

Left posterior pericardial window creation during CABG is done by the operating surgeon in the Adult Cardiac Operation Theatre of SCTIMST, Thiruvananthapuram-11.

Specify if procedure involves banking of biological samples, HIV testing, genetic testing:

No.

3) Data Analysis: The data analysis was done by the statistician employed for the purpose. Categorical and quantitative variables were expressed as frequency (percentage) and mean $\pm$ standard deviation respectively. Independent t test was used to compare quantitative parameters between categories. Chi-square test was used to find association between categorical variables. For all statistical interpretations, $p < 0.05$ was considered the threshold for statistical significance. Statistical analyses was performed by using a statistical software package SPSS, version 20.0.

RESULTS

Age:

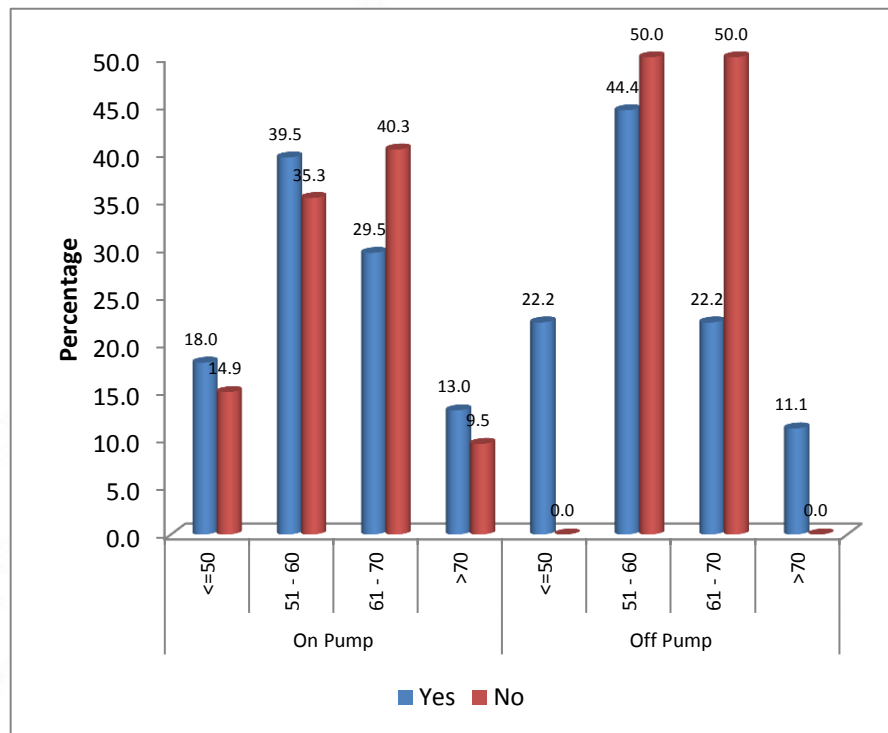
On-Pump CABG: Out of 495 patients who underwent on-pump CABG, 80 patients were aged 50 years and less (16.1%), 183 patients were aged 51-60 years (36.9%), 178 patients were aged 61-70 years (35.9%) and 54 patients were aged more than 70 years (10.9%).

- ***Mean age of the patients who had pericardial window created: 59.3 ± 9.4 years***
- ***Mean age of the patients who didn't have pericardial window created: 59.5 ± 8.6 years***

Off-Pump CABG : Out of 22 patients who underwent off-pump CABG, 4 patients were aged 50 years and less (18.1%), 10 patients were aged 51-60 years (45.4%), 6 patients were aged 61-70 years (27.2%) and 2 patients were aged more than 70 years (9.1%).

- ***Mean age of the patients who had pericardial window created : 58.6 ± 9.5 years***
- ***Mean age of the patients who didn't have pericardial window created : 61 ± 3.8 years***

Fig.1 Comparison of age based on pericardial window

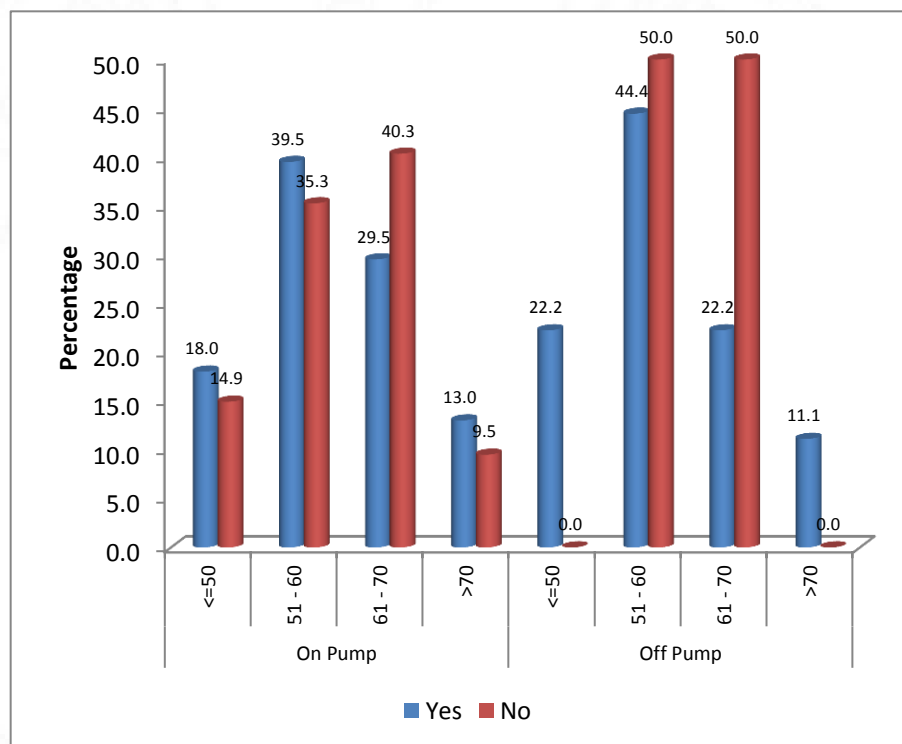


Sex:

On-Pump CABG : Out of 495 patients who underwent on-pump CABG, 434 patients were males (87.6%) and 61 were females (12.3%).

Off-Pump CABG: Out of 22 patients who underwent off-pump CABG, 19 were males (86.3%) and 3 were females (13.6%).

Fig. 2 Comparison of sex based on pericardial window



LV Ejection Fraction (EF):

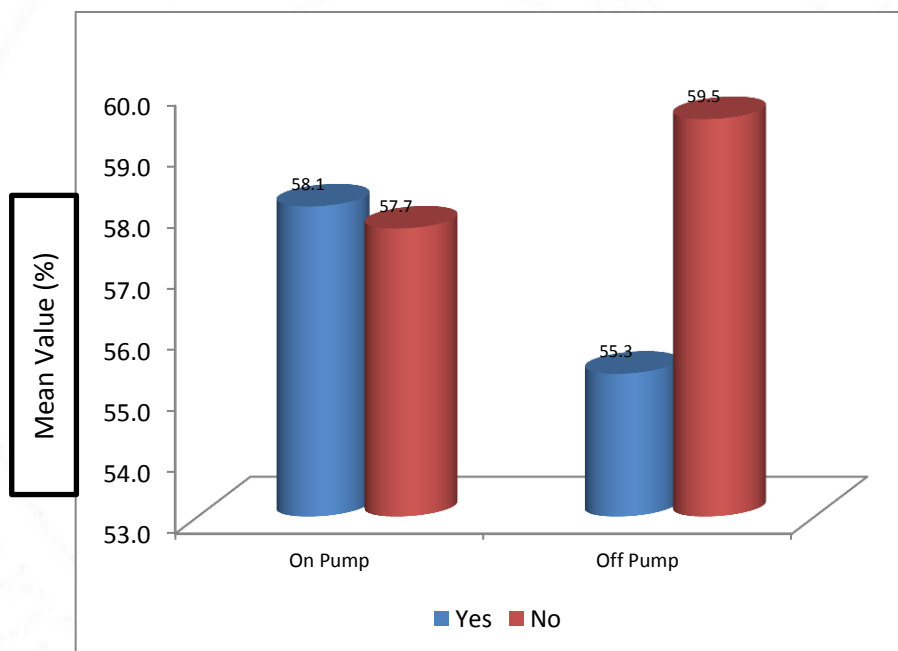
On-Pump CABG:

- Mean EF of patients who had pericardial window created : 58.1%
- Mean EF of patients who didn't have pericardial window created : 57.7%

Off-Pump CABG:

- Mean EF of patients who had pericardial window created : 55.3%
- Mean EF of patients who didn't have pericardial window created : 59.5%

Fig.3 Comparison of EF based on pericardial window



Hemoglobin Levels:

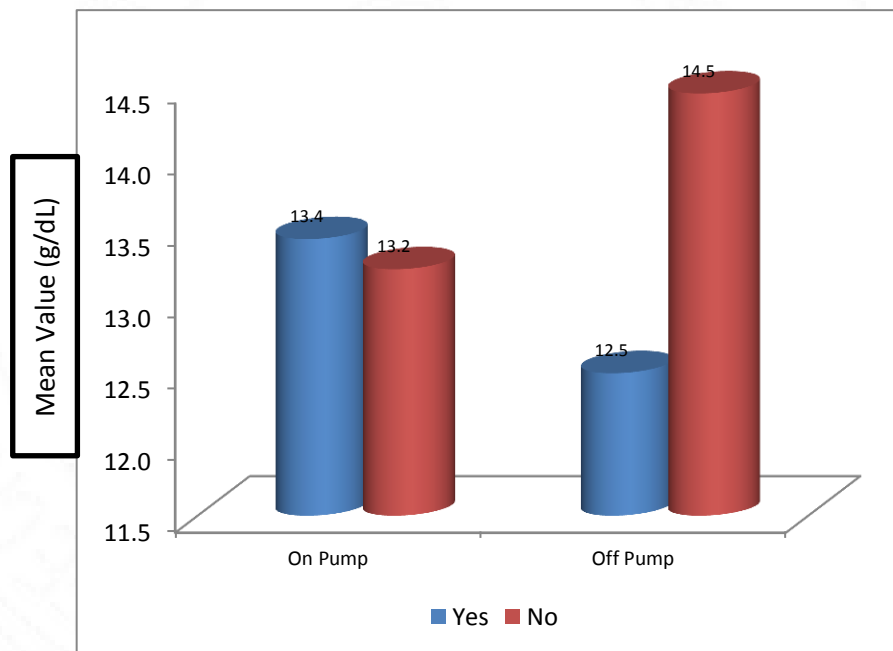
On-Pump CABG:

- Mean Hb of patients who had pericardial window created: 13.4g/dL
- Mean Hb of patients who didn't have pericardial window created: 13.2g/dL

Off-Pump CABG :

- Mean Hb of patients who had pericardial window created: 12.5g/dL
- Mean Hb of patients who didn't have pericardial window created: 14.5g/dL

Fig.4 Comparison of Hb based on pericardial window



Effect of Pericardial Window on Atrial fibrillation:

On-Pump CABG:

Total number of on-pump CABG cases: 495

- *Number of patients in which pericardial window was created: 200 (40.4%)*
- *Number of patients who developed AF after pericardial window creation: 27*
- *Percentage of patients who developed AF after pericardial window creation: 13.5%*
- *Number of patients in which pericardial window was not created: 295 (59.6%)*
- *Number of patients who developed AF without pericardial window creation: 63*
- *Percentage of patients who developed AF without pericardial window creation: 21.4%*

Table 1 Comparison of Atrial Fibrillation based on Pericardial Window in On-Pump CABG							
Coronary Artery Bypass Grafting	Atrial Fibrillation	Pericardial window				χ^2	p
		Yes		No			
		Count	Percent	Count	Percent		
On Pump	Yes	27	13.5	63	21.4	4.94*	0.026
	No	173	86.5	232	78.6		

Postoperative AF was found to be statistically significantly lower in the pericardial window patients than patients without pericardial window in patients undergoing on-pump CABG

Off-Pump CABG:

Total number of off-pump CABG cases: 22

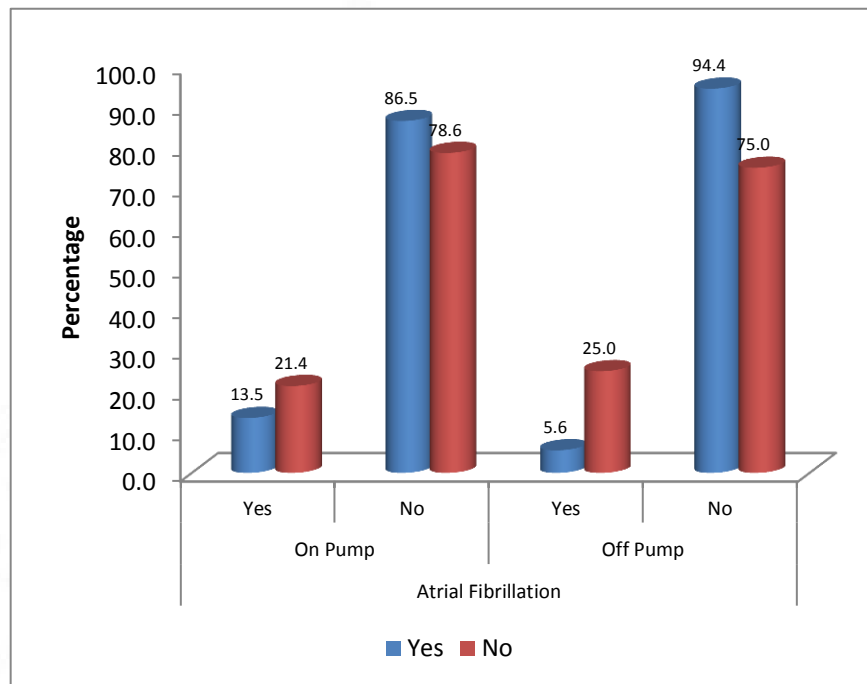
- Number of patients in which pericardial window was created: 18 (81.8%)
- Number of patients who developed AF after pericardial window creation: 1
- Percentage of patients who developed AF after pericardial window creation: 5.6%
- Number of patients in which pericardial window was not created: 4 (18.2%)
- Number of patients who developed AF without pericardial window creation: 1
- Percentage of patients who developed AF without pericardial window creation: 25%

Table 2 Comparison of Atrial Fibrillation based on pericardial window in Off-Pump CABG

Coronary Artery Bypass Grafting	Atrial Fibrillation	Pericardial window				χ^2	p
		Yes		No			
		Count	Percent	Count	Percent		
Off Pump	Yes	1	5.6	1	25.0	1.5	0.221
	No	17	94.4	3	75.0		

Postoperative AF was found to be not statistically significantly lower in the pericardial window patients than patients without pericardial window in patients undergoing off-pump CABG even though the prevalence of AF was lower in the pericardial window patients

Fig. 5 Comparison of Atrial Fibrillation based on pericardial window



Comparison of Mortality/Survival with Pericardial Window:

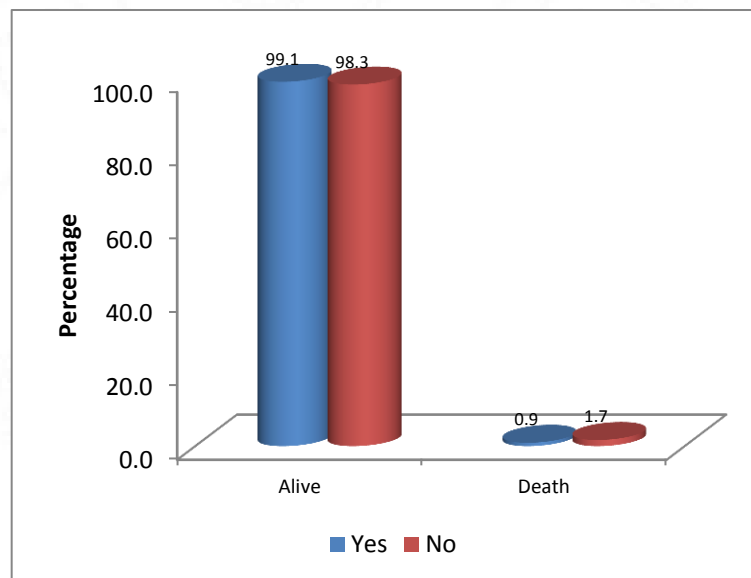
- Total number of patients studied: 517 (495 on-pump and 22 off-pump)
- Total number of pericardial window created :218 (200 on-pump and 18 off-pump)
- Total number of patients in which pericardial window was not created : 299
- Number of patients who died after creation of pericardial window: 2
- ***Percentage of patients who died after creation of pericardial window :***
 $2/218 = 0.9\%$

Number of patients who died without creation of pericardial window: 5

- ***Percentage of patients who died without creation of pericardial window:***
 $5/299 = 1.7\%$

Table 3 Comparison of Mortality/Survival based on Pericardial Window

Outcome	Pericardial window				χ^2	p
	Yes		No			
	Count	Percent	Count	Percent		
Alive	216	99.1	294	98.3	0.54	0.463
Death	2	0.9	5	1.7		

Fig.6 Comparison of Mortality/Survival based on Pericardial Window

No survival benefit was noted in patients who underwent CABG (on-pump and off-pump) with posterior pericardial window creation.

Comparison of Post-Operative Hospital Stay of Patients with Pericardial Window:

On-Pump CABG :

- Mean duration of Post-operative hospital stay in patients with pericardial window: 6.9 days
- Mean duration of Post-operative hospital stay in patients without pericardial window: 7.3 days

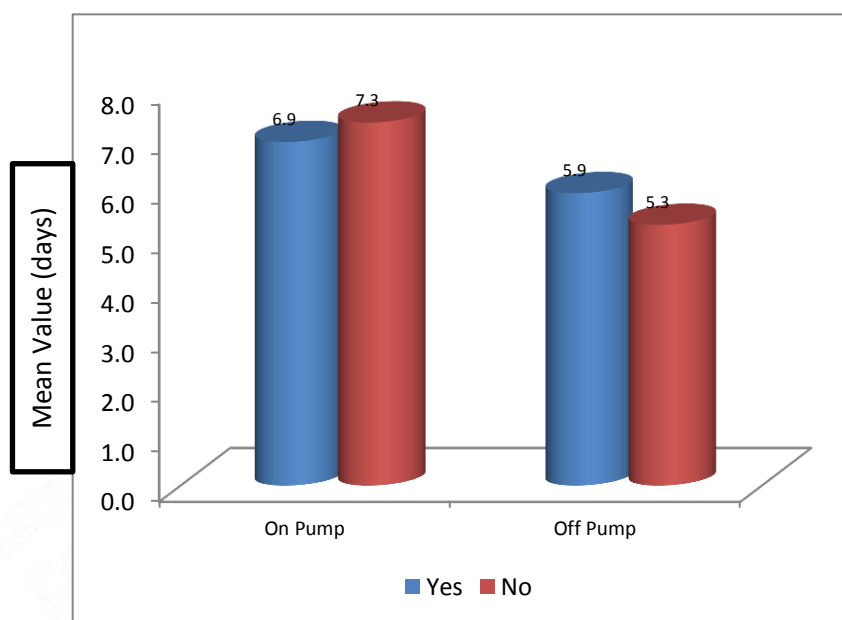
Off-Pump CABG :

- Mean duration of Post-operative hospital stay in patients with pericardial window: 5.9 days
- Mean duration of Post-operative hospital stay in patients without pericardial window: 5.3 days

Table 4 Comparison of duration of hospital stay based on pericardial window

Coronary Artery Bypass Grafting	Pericardial window						t	p
	Yes			No				
	Mean duration of hospital stay (days)	SD	N	Mean duration of hospital stay (days)	SD	N		
On Pump	6.9	4.5	200	7.3	4.1	295	1.01	0.315
Off Pump	5.9	0.9	18	5.3	0.5	4	1.36	0.190

Fig.7 Comparison of duration of hospital stay based on pericardial window



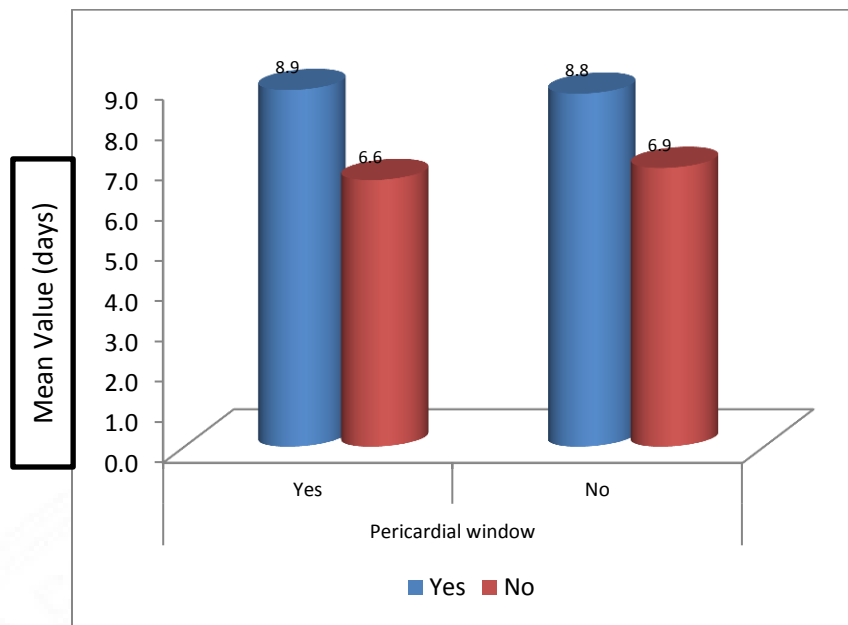
No statistical difference was noted in the duration of post-operative hospital stay in patients who had pericardial window and those who did not have pericardial window irrespective of whether it was on-pump or off-pump CABG

Table 5 Comparison of Post-Operative Hospital Stay of Patients based on AF and Pericardial Window (On –Pump CABG) :

Pericardial window	Atrial Fibrillation						t	p
	Yes			No				
	Mean duration of hospital stay (days)	SD	N	Mean duration of hospital stay (days)	SD	N		
Yes	8.9	3.9	27	6.6	4.5	173	2.45*	0.015
No	8.8	4.5	63	6.9	3.9	232	3.2**	0.002

**:- Significant at 0.01 level, *:- Significant at 0.05 level

Fig. 8 Comparison of duration of hospital stay based on AF and presence of Pericardial window among on- pump CABG



Mean duration of hospital stay in patients who had pericardial window and developed AF (8.9 days) was found to be significantly higher than patients who had pericardial window and did not develop AF (6.6 days). Also mean duration of hospital stay in patients who did not have pericardial window and developed AF (8.8 days) was significantly higher than patients who didn't develop AF (6.9 days)

DISCUSSION

New-onset AF is widely known to increase morbidity after cardiac surgery, and several studies have shown increased in-hospital and long-term mortality. But this association is not well established or clearly understood. However, other studies have not reported new-onset AF to have an independent effect on in-hospital mortality. Additionally, information related to new-onset AF comes mostly from single-institution studies.

In our study, mortality benefit was not observed in the creation of pericardial window for preventing POAF. Percentage of patients who died after creation of pericardial window was found to be 0.9% while percentage of patients who died without creation of pericardial window was 1.7%. The latest RCT study published by Guadino et al.²⁴ also says no mortality benefit for the procedure but significant reduction on POAF was noted with pericardial window group.

In our study, significant reduction in POAF was seen in the pericardial window group than no intervention group in on-pump CABG cases. Percentage of patients who developed AF after pericardial window creation was 13.5% while percentage of patients who developed AF without pericardial window creation was 21.4%. According to the systematic review and metaanalysis published by Gozdek et al.¹²⁸, posterior pericardial drainage significantly reduced the odds of POAF by 58% ($P < .001$). It is one of the largest databases that analyzes the potential beneficial value of a posterior pericardial drainage after heart surgery.

While POAF was found to be significantly lower in the pericardial window group than no-pericardial window group undergoing on-pump CABG ($\chi^2 = 4.94$, $p = 0.026$), this difference was not seen in off-pump CABG group ($\chi^2 = 1.5$, $p = 0.221$). On-pump CABG involves right atrial incision for cannulation purpose in need for cardiopulmonary bypass. The atrial incision/atriotomy can be a potential risk factor for atrial inflammation and fibrosis which can lead to postoperative arrhythmias/AF.^{103-106,109} This may partially explain the finding in our study.

Duration of hospital stay was also seen to be higher in patients who developed POAF than who did not in our study. It is universally documented in all previous studies related to POAF. With pericardial window creation, mean duration of hospital stay decreased from 8.9 days to 6.6 days in patients who developed POAF and those who didn't respectively. Such a decrease of the mean duration of postoperative hospital stay has significant economic impact in the lives of patients. It is one of those salient but strong factors that should propel the surgeons' community to choose pericardial window as standard of care during CABG.

Mechanisms of Post-Operative AF:

In their manuscript in *"Heart"*, Filardo and colleagues report on the incidence of post-CABG AF using data collected from five high-volume centres in the USA. The authors found that the unadjusted incidence of post-CABG AF was around 29.5% and 33.1% after adjustment for comorbidities captured using the Society for Thoracic Surgery score. The incidence of post-CABG AF did not significantly change over the study period which spanned from 2002 to 2010. The median time of onset of AF after CABG was 52 hours and the first episode lasted for an average of 7.2 hours.²⁵

The study found some expected differences in the prevalence of cardiovascular comorbidities in patients who did and those who did not develop post-CABG AF. These include age, male sex, white race, hypertension, vascular disease, smoking, cerebrovascular disease and others. These same risk factors are associated with AF in the general population. Weight loss has been shown to reduce the burden of AF in obese patients. It is notable that no difference in body mass index was seen in this cohort between patients who developed post-CABG AF and those who did not.

The left atrium has been the focus of attention in identifying triggers and a substrate for AF. On-pump surgery requires cannulation for cardiopulmonary bypass and this can be done through the right atrium or the vena cava. CABG does not typically require significant manipulation of the left atrial substrate. Therefore, the pathophysiology behind the high incidence of new-onset post-CABG AF is not completely understood. It is likely, however, that post-CABG AF shares common mechanisms with AF that is not associated with surgery. These include the firing of

electrical triggers, a **vulnerable atrial substrate** composed of both electrical and structural tissue remodeling, all in the presence of a **proarrhythmic autonomic milieu**.

In a study by Yaksh et al²⁶, episodes of AF in a post-CABG population were noted to be preceded by an increase in the heart rate and the frequency of premature atrial depolarizations. The increase in heart rate is typically due to a combination of vagal withdrawal and sympathetic stimulation. This shift in autonomic balance is also accompanied by an increase in heart rate variability.²⁷ Tightly coupled premature atrial beats in this autonomic milieu are more likely to induce AF.

Acute electrical repolarisation changes have been demonstrated to contribute in creating an electrical substrate for AF and have been observed after CABG. A wider dispersion of the atrial effective refractory period has been demonstrated by Soylu and colleagues following CABG.²⁸ This change in the electrical properties of the atrial tissue is an indicator of heterogeneity in atrial electrical excitability, which increases the propensity for fibrillation.

Ischemic heart disease can contribute to the creation of an atrial fibrotic substrate for AF through atrial ischemia or infarction. Indeed, human and animal studies show that infarctions involving atrial branches of the right coronary artery and left circumflex branches of the left coronary artery are associated with later onset AF.²⁹ Elevated inflammatory markers, such as soluble vascular cell adhesion molecule 1, have also been associated with new-onset post-CABG AF indicating a contribution from a systemic inflammatory process.³⁰

Postoperative AF, following either cardiac or non-cardiac surgery, is strongly associated with later recurrences of the arrhythmia, temporally removed from the acute surgical changes discussed above.³¹ This suggests that autonomic changes, electrical dispersion and a tissue substrate for AF may already exist preoperatively and likely continue to develop postoperatively. Morphological changes including increase in atrial size and P wave prolongation on 12-lead ECGs have been shown to be associated with new-onset AF following CABG.³² Similar associations of P wave duration and atrial size have been made with new-onset, non-postoperative AF.³³ These morphological changes reflect an underlying tissue change of which atrial fibrosis is a major component. Clinical risk factors, including advanced age, systemic

hypertension, diabetes, ischemic heart disease, heart failure and sleep apnoea, are also associated with atrial fibrosis in patients with AF.³⁴ Interventions aimed at risk factor control including hypertension, obesity and sleep apnoea have been shown to reduce the burden of AF.³⁵ Whether these interventions, including treating ischemic heart disease through revascularisation after CABG, reverse or slow the progression of fibrosis in human atria needs further studies.

Conceptual Model of AF Mechanism:

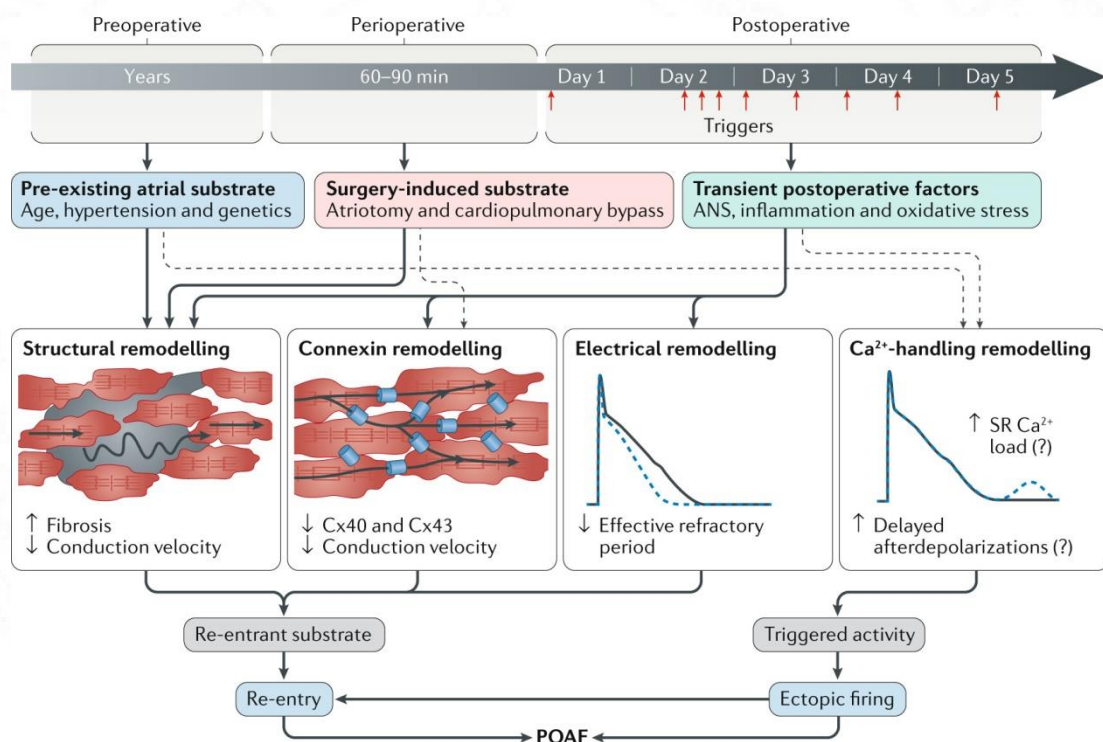
In the normal atrium, re-entry is not sustained; a vulnerable substrate resulting from changes in refractoriness and/or conduction abnormalities is needed to maintain re-entry. Ectopic firing is often needed to induce re-entry in the presence of a vulnerable substrate and can by itself maintain AF if the ectopic firing is sustained, rapid and associated with fibrillatory conduction. In the model shown in Fig. 9, POAF occurs when transient, postoperative triggers act on a vulnerable atrial substrate produced by preoperative, surgery-induced and postoperative remodelling processes favouring the two main arrhythmogenic mechanisms: ectopic firing due to **triggered activity** and **re-entry**. Triggered activity is promoted by excessive prolongation of repolarization leading to early after depolarizations or by Ca²⁺-handling abnormalities leading to spontaneous diastolic Ca²⁺ releases from the sarcoplasmic reticulum (SR) and delayed afterdepolarizations.³⁶ Triggered firing often preferentially occurs around the pulmonary veins owing to the electrophysiological and structural properties of this region, but non-pulmonary-vein triggers can also initiate AF.³⁷ The AF re-entrant substrate is characterized by short refractory periods and/or conduction abnormalities resulting from structural remodelling or impaired electrical cell-to-cell coupling via gap junctions. In this conceptual model, POAF is promoted by factors inducing atrial arrhythmogenic remodelling before surgery as well as (transient) factors increasing the substrate vulnerability or the type and number of triggers postoperatively. Activation of the autonomic nervous system and inflammation are the principal transient factors associated with cardiac surgery that initiate POAF, whereas the preoperative atrial substrate largely results from tissue-structure changes that impede atrial conduction.³⁸

An increase in sinus rate and atrial ectopic activity, pointing to an increased

sympathetic tone, often precede POAF.^{39,40} Elevated postoperative blood noradrenaline concentrations are independently associated with POAF occurrence.⁴¹ Drugs that increase sympathetic tone also increase the incidence of POAF^{42,43}, whereas perioperative β -blocker use reduces the incidence of POAF.^{44,45} The baseline magnitude of intrinsic cardiac-nerve activity also correlates with the burden of premature atrial contractions and the development of POAF.⁴⁶ In addition, the incidence of POAF is lower after cardiac transplantation, which denervates the heart, than after other forms of cardiac surgery.⁴³

Sympathetic drive is accompanied by increased vagal tone⁴⁷, and pharmacological denervation with botulinum toxin prevents POAF⁴⁸, pointing to combined sympathovagal triggering of POAF.⁴⁷ Sympathetic drive also activates the renin–angiotensin–aldosterone system. Preoperative plasma aldosterone levels are higher in patients with POAF than in patients without POAF, pointing to a potential contribution of the renin–angiotensin–aldosterone system.^{49,50}

Figure 9



Preoperative and postoperative white blood cell counts are higher in patients with POAF than in controls, and the timing of peak counts coincides with the onset of POAF.^{51–55} Similarly, the time course of AF after cardiac surgery corresponds roughly to changes in inflammatory markers.³⁸ For example, elevated preoperative plasma

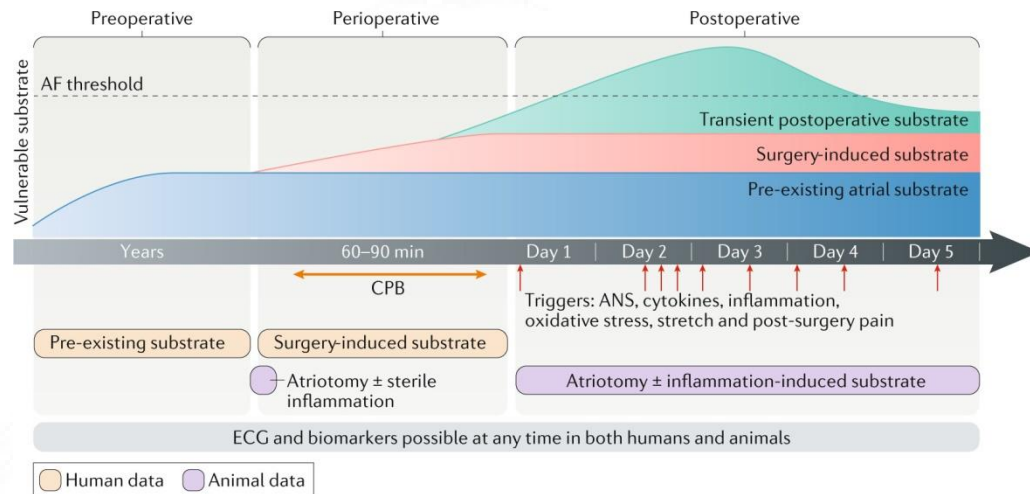
levels of IL-2 and IL-6, which are important cytokines mediating inflammatory responses, are reported in some⁵⁶⁻⁵⁹ but not all^{60,61} studies of patients with POAF. Similarly, postoperative IL-6 levels are associated with POAF in some studies^{58,62,63} but not in others.^{64,65} Most studies show a lack of association between preoperative C-reactive protein levels and POAF.⁶⁶ Postoperative activation of C-reactive protein has been associated with POAF occurrence³⁸, but contradictory data again exist^{52,56,67,68}. Corticosteroids might reduce the incidence of POAF by inhibiting cytokine release⁶⁹, consistent with an inflammatory component. Inflammation causes conduction disturbances that facilitate re-entry.⁷⁰ Overall, these findings point to a contribution of inflammation. The inconsistent results for blood biomarkers might be due to a primary role of local inflammation affecting the atria.⁷¹⁻⁷³

Cellular Mechanisms:

Atrial tissue samples taken from patients at the start or end of cardiac surgery provide useful insights about the pre-existing atrial substrate and surgery-induced substrate predisposing to POAF development in response to postoperative triggers, respectively (Fig. 10). However, these studies cannot address the mechanisms that directly cause POAF because the tissues are not harvested at the time of arrhythmia development, which is several days after the surgery. Conversely, studies in animal models to address the mechanisms of POAF typically create only an atriotomy to simulate cardiac surgery, thereby ignoring the complex effects of cardiac surgery in patients (such as atrial ischaemia during aortic cross-clamping and the effects of extracorporeal circulation) (Fig. 10). Studies of the pre-existing atrial substrate have involved atrial appendage tissue from patients in sinus rhythm with no preoperative history of AF who develop POAF compared with those who remain in sinus rhythm during the postoperative period. The large majority of the studies of human atrial samples to assess the pre-existing atrial substrate have been performed in right atrial (RA) appendage tissue, with only a few studies using LA tissue as well. Although these tissue samples reflect the best that can routinely be obtained in patients undergoing cardiac surgery, these samples might not be representative of the entire atria. For example, the LA posterior wall and pulmonary veins have a different embryological origin from that of the atrial appendages.⁷⁴ As such, the failure to

identify differences in atrial remodelling between patients with and those without POAF might be due to limitations of available tissue sampling.

Figure 10



Determinants of Ectopic Firing in Atrial Samples of patients with POAF:

Ca^{2+} handling remodelling that promotes ectopic firing is a typical finding in patients with paroxysmal⁷⁵ and longstanding persistent (chronic)⁷⁶ AF. Whether preoperative abnormalities in cardiomyocyte Ca^{2+} handling are involved in POAF is currently unclear. Previous work has reported either increased⁷⁷ or unchanged⁷⁸ L-type Ca^{2+} current ($\text{I}_{\text{Ca,L}}$) in POAF, along with similar mRNA levels of the poreforming Cav1.2 subunit.^{79,80} The $\text{I}_{\text{Ca,L}}$ response to β -adrenergic receptor stimulation is also similar in patients with and those without POAF⁷⁸, consistent with unchanged β 1-adrenergic receptor and β 2-adrenergic receptor expression.⁷⁹ The mRNA levels encoding the sarco/endoplasmic reticulum Ca^{2+} ATPase type 2a (SERCA2a) are either unchanged⁷⁹ or reduced⁸¹ in POAF, whereas protein levels of SERCA2a are similar to those in hearts in sinus rhythm.⁸¹ The mRNA or protein abundance of the SERCA2a inhibitor phospholamban (PLB), ryanodine receptor 2 (RyR2), the RyR2 regulator triadin, inositol 1,4,5-trisphosphate receptor type 3 (IP3R3) and $\text{Na}^+/\text{Ca}^{2+}$ exchanger 1 (NCX1) is similar in patients with and those without POAF.^{79,81} By contrast, the mRNA and protein levels of the atrial-selective SERCA2a inhibitor sarcolipin are reduced in POAF, which might cause SR Ca^{2+} overload.⁸¹ Overall, the evidence does not point to important preoperative Ca^{2+} handling abnormalities in patients with POAF.

Determinants of Re-entry in Atrial Samples of Patients with POAF:

Patch clamp studies in human atrial cardiomyocytes have addressed the electrophysiological properties that differentiate patients who subsequently develop POAF from those who stay in sinus rhythm. Action potential duration and effective refractory period (ERP) are not different between patients with and those without POAF.⁷⁸ Resting membrane potential is probably also unchanged because of the unaltered expression and function of the inward-rectifier K⁺ current (IK1).^{78,80,82} The similar action potential upstroke velocity and the unaltered abundance of mRNA encoding the Na⁺-channel subunit SCN5A indicate unaltered peak Na⁺ current.^{78,79} The expression of a wide range of other ion-channel subunits does not differ between patients with POAF and those in sinus rhythm.^{79,80} Therefore, the preoperative substrate of POAF (sampled at the time of surgery) is not characterized by re-entry-promoting electrical remodelling.

Several studies indicate that POAF is associated with preoperative structural alterations including interstitial fibrosis, cellular hypertrophy and signs of cellular degeneration.³⁸ LA fibrosis is a consistent finding in patients with POAF^{80,83,84}, whereas RA fibrosis has been reported in some^{67,85–88} but not all^{81,84,89–91} studies. Impaired atrial autophagy⁹¹, increased or unchanged apoptosis together with increased levels of apoptosis-inducing factor protein^{65,87,90,92} and cardiomyocyte hypertrophy⁸⁷ have also been described, whereas ubiquitylation is unchanged.⁹¹ Similarly, RA and LA fat infiltration is not different between patients with and those without POAF.⁸⁰

The molecular basis of the preoperative alterations in extracellular matrix components is poorly understood.³⁸ LA fibrosis in patients with POAF is associated with increased levels of mRNAs encoding type I collagen and type III collagen and the profibrotic stimuli transforming growth factor- β (TGF β) and angiotensin II⁸⁴, although a lack of change in type I collagen expression has also been reported.^{80,89} Protein levels of the leucin-rich proteoglycan decorin, which negatively regulates cardiac growth and collagen fibrillogenesis, are reduced in POAF.⁹³ RA expression of the atrial-selective, profibrotic stimulus connective tissue growth factor⁹³, type 1 and type 2 angiotensin II receptors⁷⁹ and extracellular matrix biglycans is unchanged in POAF.⁹³ Atrial protein levels of transferrin are upregulated, implicating iron metabolism changes and associated inflammation in POAF.⁶⁵ Although the mRNA

levels of ACTC1 and ACTA2 are similar in both groups⁸⁰, protein levels of cytoskeletal desmin are reduced in POAF⁶⁵, and increased myocytolysis has been reported in patients with POAF.⁸⁷ RA tissue from patients with POAF has reduced mRNA expression of the myosin heavy chain gene MYH6⁸¹, which might cause both sarcomere derangement and functional impairment, and a loss of sarcomere organization has been reported in patients with POAF.⁹¹ The mRNA and protein levels of the connexins responsible for atrial intercellular electrical coupling (connexin 40 and connexin 43; also known as gap junction- α 5 protein and gap junction- α 1 protein, respectively) are unchanged in POAF^{79,85}, pointing to structural alterations as the most likely cause of re-entry-promoting heterogeneous conduction in patients with POAF.

Upstream factors contributing to the substrate for POAF on the basis of results from human atrial samples:

Differences in levels of upstream factors, including reactive oxygen species (ROS), inflammation and autonomic dysfunction, observed in human atrial samples obtained at the start of surgery influence both the re-entry-promoting substrate and ectopic firing. In addition, upstream factors can alter the atrial response to transient postoperative changes, making the initiation of POAF more or less likely. Levels of ROS, which increase both ectopic activity and the re-entry substrate⁹⁴, are increased in the atria of patients who are prone to develop POAF.⁹⁵⁻⁹⁷ A variety of associated changes have been reported. Levels of NADPH oxidase-derived and monoamine oxidase-derived superoxide anion (O_2^-) and peroxynitrite ($ONOO^-$) are both increased in the right atria of patients with POAF.⁹⁵⁻⁹⁷ Patients with POAF have an increase in RA basal superoxide release, which has been associated with an increased tissue protein level of monoamine oxidase⁹⁵, as well as gp91phox (NOX2) and p22phox subunits of NADPH oxidase.⁹⁶ In the same tissue samples, levels of integrin- β 2 (CD18) did not differ between patients with and those without POAF, indicating that differences in neutrophil infiltration do not account for the increase in NOX2 activity in patients with POAF and that NADPH oxidase activity in atrial cardiomyocytes might have a role in the development of POAF.⁹⁶ Tetrahydrobiopterin (BH4) levels are preserved in POAF, rendering uncoupling of

nitric oxide synthase unlikely⁹⁶, whereas the protein abundance of the antioxidant peroxiredoxin 1 is reduced.⁶⁵ The expression of the antioxidants glutathione, glutathione peroxidase and glutathione reductase is unchanged in POAF⁹⁵, and global pre-surgical mitochondrial function is normal in patients with and those without POAF.⁹⁸

No clear differences in macroscopic inflammation, such as more immune cell infiltrates, have been observed in the atrial tissue of patients with and those without POAF.^{87,90,91,96} Nevertheless, two studies have shown that the protein levels of nuclear factor- κ B (NF- κ B) are increased in atrial tissue of patients with POAF.^{71,85}

NF- κ B expression increases with angiotensin II stimulation, and elevated plasma angiotensin II levels are independently associated with POAF.⁹⁹ Higher NF- κ B protein levels and increased ROS production should prime and trigger the activation of the NLRP3 inflammasome¹⁰⁰, the components of which are upregulated in the atrial tissue of patients with POAF.⁷¹ In addition, levels of circulating mitochondrial DNA, which can activate the NLRP3 inflammasome in cardiomyocytes via Toll-like receptor–NF- κ B pathway stimulation, strongly increase after surgery at the time of peak onset of POAF.⁶³ These data position abnormal atrial inflammatory signalling as an important potential contributor to POAF.

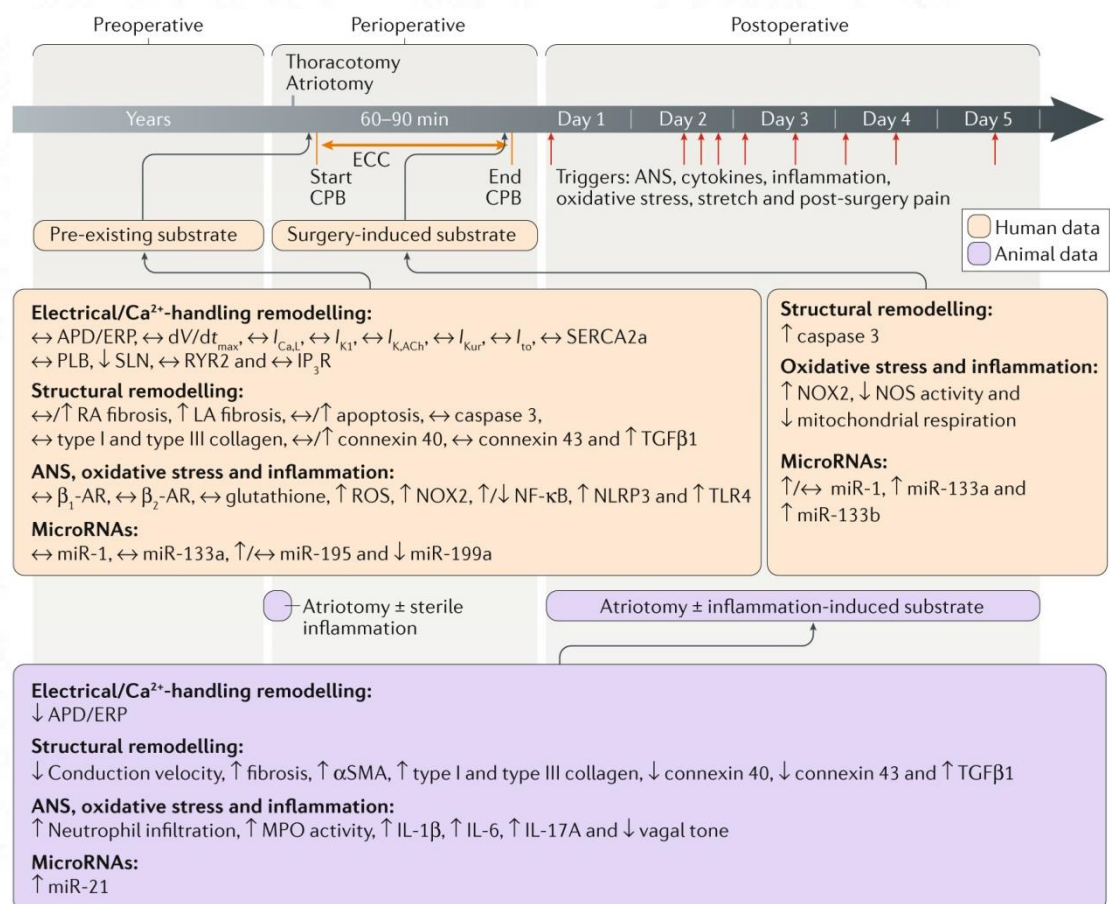
The cellular mechanisms by which autonomic dysfunction promotes POAF have not been elucidated. Sympathovagal activity might shorten the action potential duration (parasympathetic effect) in combination with increased and prolonged intracellular Ca²⁺ transients (sympathetic effect). The increased intracellular concentration of Ca²⁺ during final action potential repolarization can generate a depolarizing current mediated by NCX1, causing early after depolarizations and triggered activity.⁹⁶ To distinguish these early after depolarizations from the classic forms induced by reactivation of I_{Ca,L}, they have been termed late phase 3 early afterdepolarizations.¹⁰¹ Alternatively, spontaneous diastolic SR Ca²⁺-release events, promoted by increased SR Ca²⁺ load and hyperphosphorylation of RYR2 channels during sympathetic stimulation, might cause delayed afterdepolarizations. Although these possibilities are compelling, they remain speculative pending direct evidence. Several additional similarities and differences in transcription factors, microRNAs, structural proteins and proteins involved in metabolism and apoptosis have been

identified between atrial samples from patients with and those without POAF¹⁰², but their relevance to postoperative atrial arrhythmogenesis is largely unknown.

Role of Atrial Ischaemia:

Surgery-related ischaemia has been suggested to sensitize the preoperative atrial substrate to postoperative AF triggers. A few studies have managed to collect atrial samples just before and after aortic cross-clamping, allowing signs of atrial ischaemia–reperfusion to be analysed^{103–106} (Fig. 11).

Figure 11



Mitochondrial function is closely linked to arrhythmogenesis through the generation of ROS and the modulation of Ca²⁺ homeostasis.¹⁰⁷ A reduction in human atrial mitochondrial respiration (oxidative phosphorylation), with no evidence for selective deficits in any specific component of the electron transport chain, has been

identified in response to aortic crossclamping.¹⁰³ In agreement, preoperative to postoperative differences in inflammatory markers, protein oxidation and regulators of oxidative stress and atrial metabolism are more pronounced in patients with POAF than in those without POAF.¹⁰⁵ These data are consistent with the impaired mitochondrial response of human atria to simulated ischaemic injury observed in vitro.⁹⁸ Impaired mitochondrial respiration is associated with an upregulation in the atrial expression of miR-1, miR-133a and miR-133b¹⁰³, although expression of miR-1 and miR-133a was unchanged in a different study.¹⁰⁶

Conversely, in RA biopsy samples taken before aortic cross-clamping and after reperfusion, caspase activity and the BAX:BCL2 mRNA ratio increase, whereas phosphorylation of BCL-2 decreases, suggesting promotion of apoptosis.^{105,106} These changes are more pronounced in patients with POAF suggesting that surgery-induced apoptosis might contribute to the development of POAF. Interestingly, aortic cross-clamping has no effect on the plasma levels of cardiac muscle troponin T, creatine kinase M-type/B-type (CK-MB), N-terminal pro-B-type natriuretic peptide, C-reactive protein or white blood cell count up to the first postoperative day, suggesting only slight tissue damage and no early increase in cardiac inflammatory response.¹⁰³

In paired RA samples obtained before venous cannulation and after myocardial reperfusion, atrial O₂⁻ production increases significantly after reperfusion because of increased mitochondrial and NOX2 activity.¹⁰⁴ Atrial content of antioxidant BH4 and nitric oxide synthase activity also decrease after reperfusion.¹⁰⁴ Although the relationship between mitochondrial function, ROS production and POAF incidence was not studied, impaired mitochondrial function and increased ROS generation in response to ischaemia–reperfusion are very likely to sensitize the atria to develop POAF. Finally, total and phosphorylated RA protein levels of connexin 40 and connexin 43 are significantly reduced after aortic cross-clamping; however, no significant association with the incidence of POAF exists.⁸⁵

Studies in Animal Models:

The limitations of available animal models of POAF make the selection of experimental systems to study the underlying mechanisms of POAF difficult. With the exception of two studies simulating the effects of pericardiotomy (as in off-pump CABG surgery) or atriotomy (as in on-pump CABG surgery) on atrial function, the majority of studies performing atriotomy subsequently applied sterile talc to the pericardial surfaces of the atria, thereby inducing sterile pericarditis. Nevertheless, animal models enable direct access to cardiac tissues at the time of POAF, which is impossible clinically, and therefore provide valuable information complementary to clinical data.

At three days after surgery with pericardiotomy or right atriotomy, previously normal animals show increased heterogeneity in atrial conduction and greater inducibility of AF than that shown by control animals.¹⁰⁸ These electrophysiological abnormalities are associated with increases in RA neutrophil infiltration, along with increased myeloperoxidase activity.¹⁰⁸ Moreover, the duration of AF correlates with the degree of conduction inhomogeneity and atrial inflammation indices. High-dose corticosteroid treatment of dogs subjected to atriotomy suppresses POAF, indices of inflammation and changes in atrial conduction, suggesting that inflammation is an important contributor to AF induction and maintenance in this model.¹⁰⁸ The pericardiotomy and atriotomy groups also had higher postoperative heart rates owing to decreased vagal tone¹⁰⁹, which was associated with corresponding increases in atrial tissue myeloperoxidase activity and blood levels of C-reactive protein. Atrial premature beats occurred postoperatively in both groups, independent of the degree of inflammation.¹⁰⁹ These data show that atrial incision is sufficient to cause inflammation with related changes in atrial electrophysiology that promote POAF.

Sterile pericarditis in dogs, goats or rats is characterized by impaired conduction, shortened ERP and increased susceptibility to re-entrant atrial arrhythmia induction.^{70,110–115} The postoperative blood levels and atrial expression of C-reactive protein, IL-1 β , IL-6, IL-17A, tumour necrosis factor (TNF) and TGF β 1 are significantly increased in these models and are associated with epicardial thickening, leukocyte infiltration, cardiac rupture and necrosis.^{110,112–115} Corticosteroids^{116,117}, statins^{110,113}

and n-3 polyunsaturated fatty acids¹¹² prevent POAF in experimental sterile pericarditis, supporting the causal role of atrial inflammation.

With the exception of one study¹¹¹, conduction slowing is a consistent finding in sterile pericarditis.^{70,110,112} In atrial strips in which acute inflammation was induced, atrial conduction was preferentially reduced in the transverse versus longitudinal direction, which could promote the formation of re-entry circuits.¹¹¹ Pericarditis-induced conduction slowing might result from down regulation of connexin 40 and connexin 43 protein and altered physiological transmural gradients of connexin distribution, with associated intercellular coupling disturbances.⁷⁰ The gap junction modifier GAP-134 improves conduction and reduces AF burden in this model¹¹⁸, pointing to a causal contribution of connexin remodelling. Atrial fibrosis, probably a consequence of inflammatory stressors, has also been noted.^{110,114,115} This fibrosis is associated with increased mRNA expression of Acta2, Col1a1, Col3a1 and Tgfb and increased protein expression of mature and pro-matrix metalloproteinase 2 (MMP2), mature and pro-MMP9, tissue inhibitor of metalloproteinases 2 (TIMP2) and glycosylated TIMP3.¹¹⁴ Inhibition of pro-inflammatory cytokines, such as IL-17A, decreases the atrial expression of IL-6, IL-1 β and TGF β , along with the levels of type I collagen, type III collagen and α -smooth-muscle actin (α SMA), and increases the amount of MMP2 and MMP9, thereby reducing fibrosis and the duration of inducible AF episodes.¹¹⁴ In addition, atrial fibrosis is associated with increases in signal transducer and activator of transcription 3 (STAT3) phosphorylation (activation) and miR-21 expression, perhaps because of the higher IL-6 levels.¹¹⁵ Conversely, inhibition of STAT3 and application of antagomiR-21 both normalized pericarditis-induced inhomogeneous conduction and prevented AF promotion, pointing to a reciprocal feedforward regulation between STAT3 and miR-21.¹¹⁵ Therefore, cytokines might contribute to the development of AF by promoting cardiac inflammation and related atrial fibrosis.

ERP seems to be consistently shortened in sterile pericarditis^{110,112–114}, with only one study showing no significant ERP abbreviation.¹¹¹ Application of multi-ion-channel blockers, such as K201 (also known as JTV-519)^{119,120}, ranolazine¹²¹ and AZD7009¹²², and the IKr blockers E-4031, d,l-sotalol and vanoxerine^{123–126} all cause ERP prolongation and prevent AF in the sterile pericarditis paradigm. Overall, according

to the data from animal models, shorter ERP, slowed and/or heterogeneous conduction, inflammation and atrial fibrosis are likely to promote re-entry in the period after cardiac surgery.⁷⁰

Pericardial Window in Preventing POAF:

By allowing drainage of fluids that get collected in the pericardium post operatively into pleural space,pericardial window offers ***less stretch on atrial tissue*** which helps in the lower occurrence of POAF. Atrial substrate/stretch/ischemia is a prominent factor in the mechanism of development of POAF. Consequently, this manoeuvre helps in mitigating the effects of pericardial collection, one of which is postoperative atrial fibrillation.

CONCLUSION AND RECOMMENDATION:

Posterior pericardial drainage is safe and simple technique that significantly reduces the prevalence of POAF. Posterior pericardial drainage allows free escape of the fluid to the pleural space or on the outside via chest tubes and hence the chances of pericardial effusion/tamponade and consequently POAF is greatly reduced. Since it's a cost effective technique, it should be routinely employed in cardiac surgery units to reduce the complication of POAF and the related morbidity and mortality.

LIMITATIONS OF THE STUDY:

- As it is a retrospective study, it limits the assessment of perioperative complications
- It's a single centre study
- Due to marked heterogeneity of the underlying diseases, the results of the study cannot be generalized
- The number of off-pump CABG cases were low,hence results cannot be generalised

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ANNEXURE I

STUDY PROFORMA/DATA COLLECTION FORM

TITLE: Role of Intraoperative Posterior Pericardial Window in Preventing Postoperative Atrial Fibrillation in On-Pump Coronary Artery Bypass Grafting Patients

Patient ID :
Age :
Sex : M/F
Diagnosis :

Date of Surgery :

Date of Discharge :

Duration of Hospital Stay :

LVEF :

Hb% :

On-pump/Off-pump :

Alive/ Dead :

Pericardial Window : Yes/No

POAF (within 7 days of surgery) : Yes/No

ANNEXURE II

IEC APPROVAL LETTER



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
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Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1707 /August/ 2021

16.09.2021

Dr. John Mathew K
PDF, Adult Cardiac Surgery
Department of CVTS
SCTIMST, Thiruvananthapuram

Dear Dr. John Mathew,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "ROLE OF INTRAOPERATIVE POSTERIOR PERICARDIAL WINDOW IN PREVENTING POSTOPERATIVE ATRIAL FIBRILLATION IN ON-PUMP CORONARY ARTERY BYPASS GRAFTING PATIENTS (IEC/1707)" on 18th August, 2021.

The following members of the Ethics Committee were present at the meeting held on 18th August, 2021 at Residences and Offices of IEC Members via Video Conference

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Prof. C.C. Kartha	MBBS,MD	Male	Basic Medical Scientist (Chairman)	No
2.	Dr. Kala Kesavan P	MBBS,MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
5.	Dr. Achuth Sankar S. Nair	Ph.D (i.Engineering ii.Music)	Male	Social Scientist	No
6.	Dr. Rejnish Kumar	MBBS,MD ,DNB	Male	Clinician	No
7.	Adv. N Anand	BAL, L.LB	Male	Legal Expert	No
8.	Adv. Priya Kaimal	LLM, MBL	Female	Legal Expert	No
9.	Dr. Harikrishna Varma P. R	Ph.D (Materials Sciences)	Male	Medical Technology	Yes
10.	Dr. Manikandan S	MBBS,MD,PDCC	Male	Clinician	Yes
11.	Dr. Narayanan Namboodiri. K K	MBBS,MD,DM	Male	Clinician	Yes
12.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
13.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

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The following documents were reviewed:

Original submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 23.07.2021
2. IEC Application Form
3. Proposal
4. Study proforma
5. CV of PI and Co-PIs
6. Declaration Form
7. Dean's signature form

Revised submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 15.09.2021
2. IEC Application Form
3. Proposal
4. Study proforma
5. CV of PI and Co-PIs
6. Declaration Form
7. Dean's signature form

IEC Decision

The IEC approved the conduct of the study in the present form

This approval is in continuation of IEC Regn No. ECR/189/Inst/KL/2013/RR-16, subject to IEC Renewal pending process with CDSCO

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,



G. Srinivas
Member Secretary, IEC



MASTER CHART

Sl no	H: No	Date of Surgery	Pericardial window	Atrial Fibrillation	Date of Discharge/Death	Age (years)	Sex	EF (%)	Hb (g%)	Duration of Hospital Stay (days)	Remark
1	495590	5.4.21	yes	no	12.4.21	61	m	68	13.5	7	
2	495996	5.4.21	no	no	10.4.21	69	m	70	13.9	5	
3	496106	7.4.21	yes	no	12.4.21	64	m	71	15.3	5	
4	494865	7.4.21	no	no	15.4.21	63	m	56	13.8	8	
5	495997	8.4.21	yes	no	13.4.21	70	m	65	13.8	5	
6	490873	8.4.21	no	no	13.4.21	50	m	70	15.7	5	
7	487003	12.4.21	yes	no	18.4.21	55	f	43	11.5	6	
8	492615	12.4.21	no	no	23.4.21	55	m	72	15.8	11	
9	497068	12.4.21	yes	yes	28.4.21	79	m	37	11.7	16	
10	494072	13.4.21	yes	no	19.4.21	49	m	60	15.9	6	
11	496083	13.4.21	no	no	19.4.21	69	m	70	14.1	6	
12	496506	15.4.21	yes	no	20.4.21	55	m	66	15.5	5	
13	495893	15.4.21	no	yes	21.4.21	65	m	63	14	6	
14	496216	16.4.21	yes	no	21.4.21	60	m	72	15.8	5	
15	496103	16.4.21	no	no	21.4.21	55	m	58	15.1	5	
16	493566	20.4.21	yes	yes	25.4.21	67	m	60	13.3	5	
17	298761	20.4.21	no	yes	26.4.21	74	m	69	12	6	
18	496333	26.4.21	no	no	2.5.21	59	f	69	12.1	6	
19	496436	26.4.21	yes	no	1.5.21	55	m	66	14.2	5	
20	496564	4.5.21	no	no	10.5.21	36	m	38	15.7	6	
21	498111	6.5.21	yes	no	11.5.21	42	m	67	13	5	
22	497397	7.5.21	no	no	12.5.21	45	m	35	15.9	5	
23	496825	7.5.21	yes	no	12.5.21	58	m	75	15.1	5	
24	497181	10.5.21	yes	no	16.5.21	45	f	30	14.7	6	
25	494941	10.5.21	no	no	16.5.21	54	m	66	12	6	
26	497933	11.5.21	no	no	16.5.21	56	m	80	15.7	5	
27	497645	11.5.21	no	yes	17.5.21	66	m	65	15.4	6	
28	497726	12.5.21	no	yes	19.5.21	50	m	60	17.3	7	
29	465446	12.5.21	yes	no	19.5.21	38	m	60	15.3	7	
30	497802	14.5.21	no	no	21.5.21	36	m	60	17	7	
31	497350	14.5.21	yes	no	21.5.21	66	m	52	12.2	7	
32	497828	17.5.21	yes	yes	28.5.21	71	m	51	15.4	11	
33	493961	18.5.21	no	yes	25.5.21	49	m	75	15	7	
34	498013	20.5.21	no	yes	28.5.21	56	m	54	18	8	
35	496082	24.5.21	no	no	29.5.21	67	f	78	12.3	5	
36	498287	24.5.21	yes	no	31.5.21	60	m	64	14.5	7	
37	497843	25.5.21	yes	no	30.5.21	47	m	62	15	5	
38	487523	25.5.21	no	no	1.6.21	54	f	63	12.2	7	
39	497204	26.5.21	no	yes	3.6.21	76	m	35	13.2	8	death

40	495046	26.5.21	no	no	2.6.21	61	m	54	12.6	7	
41	498329	26.5.21	yes	no	31.5.21	59	m	62	13	5	
42	497724	27.5.21	yes	no	2.6.21	56	m	54	15.6	6	
43	498396	27.5.21	no	no	1.6.21	68	m	57	16.5	5	
44	467247	28.5.21	no	no	11.6.21	48	m	38	13.2	14	
45	498055	28.5.21	no	no	4.6.21	66	m	63	14.1	7	
46	497104	31.5.21	yes	no	7.6.21	71	m	54	12.7	7	
47	498596	31.5.21	no	no	5.6.21	57	f	56	12.2	5	
48	498737	7.6.21	no	no	12.6.21	40	m	50	16.4	5	
49	498662	7.6.21	yes	no	12.6.21	56	m	70	15.3	5	
50	332839	8.6.21	no	no	13.6.21	66	f	58	12.2	5	
51	498764	10.6.21	yes	no	15.6.21	46	m	61	16	5	
52	497642	10.6.21	no	no	19.6.21	47	m	70	14.3	9	
53	498952	14.6.21	yes	yes	20.6.21	64	m	63	15.3	6	
54	498924	23.6.21	no	no	28.7.21	38	f	68	12.3	35	
55	499246	28.6.21	no	no	6.7.21	57	m	53	9.9	8	
56	499391	28.6.21	yes	no	3.7.21	68	f	78	13	5	
57	492484	29.6.21	no	no	5.7.21	54	m	60	14.5	6	
58	356691	29.6.21	no	no	5.7.21	73	m	54	13.6	6	
59	340368	1.7.21	no	no	7.7.21	64	m	53	12.3	6	
60	499381	1.7.21	yes	no	7.7.21	56	m	45	9.6	6	
61	499706	2.7.21	yes	no	11.7.21	65	m	60	10.4	9	
62	499705	2.7.21	no	no	7.7.21	57	m	43	14.3	5	
63	499315	14.7.21	no	yes	19.7.21	61	m	45	9.6	5	
64	499910	15.7.21	no	no	22.7.21	64	m	40	13.3	7	
65	499863	12.7.21	no	no	20.7.21	50	m	64	12.7	8	
66	499338	12.7.21	yes	no	17.7.21	54	m	56	15.9	5	
67	499608	13.7.21	yes	no	19.7.21	48	m	50	13	6	
68	500087	13.7.21	no	no	18.7.21	57	f	55	14.2	5	
69	499315	14.7.21	no	yes	19.7.21	61	m	45	9.6	5	
70	499910	15.7.21	no	no	22.7.21	64	m	40	13.3	7	
71	500150	19.7.21	no	no	29.7.21	60	f	57	9.6	10	
72	500136	21.7.21	yes	no	27.7.21	65	m	45	9.1	6	
73	498863	21.7.21	no	yes	29.7.21	49	m	68	10.8	8	
74	500270	22.7.21	yes	no	29.7.21	50	m	53	14.1	7	
75	500221	22.7.21	no	no	27.7.21	64	m	80	13.1	5	
76	500727	26.7.21	yes	no	1.8.21	64	f	62	16.6	6	
77	500253	27.7.21	no	no	4.8.21	61	m	40	14.7	8	
78	501023	27.7.21	yes	no	1.8.21	61	m	45	15.2	5	
79	499068	28.7.21	no	yes	3.8.21	64	m	60	15.5	6	off pump
80	501107	2.8.21	yes	no	8.8.21	61	m	50	16.1	6	
81	500158	3.8.21	yes	no	11.8.21	54	m	50	11.7	8	
82	500756	3.8.21	no	no	8.8.21	71	m	60	14.3	5	
83	499889	4.8.21	no	yes	11.8.21	68	m	60	13.5	7	
84	500723	4.8.21	no	no	9.8.21	60	m	60	14.7	5	off pump
85	500524	4.8.21	yes	no	9.8.21	49	m	68	15.3	5	
86	500547	9.8.21	no	no	14.8.21	55	f	55	12.6	5	
87	500375	9.8.21	yes	no	17.8.21	77	m	65	10.6	8	
88	501193	10.8.21	no	no	15.8.21	42	m	40	14.8	5	
89	501049	11.8.21	yes	no	17.8.21	42	m	47	13.8	6	

90	500386	11.8.21	no	no	17.8.21	68	m	22	15.9	6	
91	500592	12.8.21	no	no	19.8.21	60	m	60	13.3	7	
92	498688	13.8.21	no	yes	19.8.21	54	m	54	14.3	6	
93	501219	16.8.21	no	no	21.8.21	64	m	55	15	5	
94	499251	17.8.21	yes	no	23.8.21	48	m	60	12.4	6	
95	499719	17.8.21	no	no	26.8.21	58	m	45	16.4	9	
96	496633	17.8.21	no	yes	26.8.21	66	m	47	12.3	9	
97	500901	18.8.21	yes	no	23.8.21	60	m	56	12.3	5	
98	501040	18.8.21	no	no	24.8.21	62	m	70	14.9	6	
99	501243	24.8.21	no	no	29.8.21	66	m	50	13	5	
100	299301	24.8.21	yes	no	29.8.21	73	m	60	15.1	5	
101	499523	25.8.21	yes	no	5.9.21	61	m	53	13.8	11	
102	501117	25.8.21	no	no	1.9.21	58	f	66	13.2	7	
103	501815	26.8.21	yes	yes	2.9.21	68	m	55	12.3	7	
104	352483	26.8.21	no	no	1.9.21	65	m	55	14.6	6	
105	501593	26.8.21	no	no	2.9.21	60	m	49	13.9	7	
106	501184	27.8.21	no	no	1.9.21	52	f	68	13.4	5	
107	501110	27.8.21	no	no	2.9.21	55	m	48	14.6	6	
108	500758	31.8.21	yes	no	9.9.21	71	m	58	13.1	9	
109	501047	31.8.21	no	no	5.9.21	59	m	50	15.7	5	
110	501222	31.8.21	no	no	5.9.21	56	m	52	14.4	5	off pump
111	502009	1.9.21	yes	no	6.9.21	59	m	64	13.5	5	
112	502240	1.9.21	no	yes	10.9.21	66	m	64	12.3	9	
113	502228	1.9.21	no	no	6.9.21	55	m	54	15	5	
114	501402	2.9.21	yes	yes	10.9.21	74	m	68	12.8	8	
115	501238	2.9.21	no	no	7.9.21	72	m	54	12.4	5	
116	501370	2.9.21	no	no	8.9.21	64	m	58	14.9	6	
117	500577	3.9.21	yes	no	8.9.21	56	f	35	11.2	5	off pump
118	501328	3.9.21	no	no	8.9.21	63	m	50	14.8	5	
119	493937	6.9.21	yes	no	13.9.21	54	m	52	14.8	7	off pump
120	501591	6.9.21	no	no	25.9.21	67	m	61	13.8	19	
121	500684	6.9.21	no	no	11.9.21	46	m	42	14.3	5	
122	501539	7.9.21	no	no	14.9.21	66	m	39	14.4	7	
123	501348	7.9.21	yes	no	12.9.21	62	m	33	17.1	5	
124	494473	7.9.21	no	yes	14.9.21	71	m	28	14.5	7	
125	501036	8.9.21	no	no	13.9.21	66	m	43	14	5	
126	9606544	8.9.21	yes	no	13.9.21	79	m	43	12	5	
127	499802	9.9.21	no	no	14.9.21	59	m	60	13.7	5	
128	502606	13.9.21	yes	no	19.9.21	74	m	50	10.9	6	
129	502699	13.9.21	yes	no	18.9.21	60	m	47	10.9	5	off pump
130	274257	13.9.21	no	no	20.9.21	61	f	20	15.9	7	
131	220452	14.9.21	yes	yes	21.9.21	77	m	52	14.3	7	
132	501759	14.9.21	no	no	19.9.21	64	m	56	14.6	5	
133	502491	15.9.21	yes	no	20.9.21	46	f	53	12.9	5	
134	499599	16.9.21	no	no	22.9.21	53	m	50	15	6	
135	413581	16.9.21	no	no	21.9.21	60	m	30	15.5	5	
136	500798	17.9.21	no	no	22.9.21	62	m	43	16	5	
137	496511	17.9.21	no	no	22.9.21	49	m	68	14.7	5	
138	499602	20.9.21	no	no	27.9.21	54	f	50	11.9	7	
139	502094	20.9.21	yes	no	25.9.21	56	m	50	13.8	5	

140	502293	21.9.21	yes	yes	4.10.21	69	f	62	12.8	13	
141	502334	21.9.21	no	yes	1.10.21	62	m	72	14.8	10	
142	499249	22.9.21	yes	no	27.9.21	56	m	70	14.3	5	
143	502189	22.9.21	no	no	28.9.21	50	f	54	13	6	
144	501452	23.9.21	yes	no	28.9.21	53	m	55	12.3	5	
145	502988	23.9.21	no	no	29.9.21	59	m	58	14.6	6	
146	501233	23.9.21	no	yes	29.9.21	68	m	47	15.4	6	
147	500701	24.9.21	yes	no	1.10.21	65	m	50	17.8	7	
148	502483	24.9.21	no	yes	4.10.21	71	m	66	14.1	10	
149	503861	25.9.21	no	no	3.10.21	71	f	55	12.6	8	
150	503220	27.9.21	yes	no	5.10.21	64	m	18	13.6	8	
151	502436	27.9.21	no	no	2.10.21	67	m	52	11	5	
152	502625	28.9.21	no	no	4.10.21	71	m	64	14.1	6	
153	502751	28.9.21	no	no	4.10.21	58	m	62	16.8	6	
154	502947	28.9.21	yes	no	4.10.21	70	m	54	14.1	6	
155	502962	29.9.21	yes	no	4.10.21	71	m	59	14.9	5	
156	502796	30.9.21	yes	no	5.10.21	62	m	62	15.9	5	
157	503028	1.10.21	yes	no	9.10.21	45	m	56	13	8	
158	502608	1.10.21	no	no	6.10.21	48	m	72	14.1	5	
159	503192	5.10.21	no	no	12.10.21	65	m	68	13.2	7	
160	503108	5.10.21	no	no	10.10.21	59	m	40	11.4	5	
161	503341	6.10.21	no	yes	14.10.21	66	m	79	14.7	8	
162	503461	7.10.21	no	no	13.10.21	58	f	60	12.9	6	
163	497361	8.10.21	no	yes	18.10.21	67	m	26	13.4	10	
164	503478	6.10.21	no	no	12.10.21	62	m	67	14.8	6	
165	503030	11.10.21	no	no	16.10.21	61	m	65	15.9	5	
166	336100	11.10.21	no	no	16.10.21	40	m	40	10.5	5	
167	504791	13.10.21	no	no	21.10.21	57	f	63	13.9	8	
168	325025	13.10.21	no	yes	20.10.21	67	m	60	12.7	7	
169	503673	18.10.21	yes	yes	27.10.21	65	m	53	14.6	9	
170	504400	18.10.21	no	no	23.10.21	57	m	52	14.3	5	
171	504860	20.10.21	yes	no	25.10.21	65	m	47	9.8	5	
172	503858	20.10.21	no	no	25.10.21	72	m	73	14	5	
173	504642	21.10.21	no	yes	29.10.21	61	m	53	14.5	8	
174	504303	21.10.21	yes	no	29.10.21	49	m	74	14.7	8	
175	492659	25.10.21	yes	yes	1.11.21	71	m	55	14.1	7	
176	503725	26.10.21	yes	no	2.11.21	45	m	69	15.5	7	
177	503705	26.10.21	yes	no	1.11.21	57	m	57	13.1	6	
178	504329	27.10.21	yes	no	2.11.21	67	m	60	14.7	6	
179	503469	28.10.21	yes	no	3.11.21	62	m	60	14.5	6	
180	500462	28.10.21	yes	no	2.11.21	55	m	46	15.4	5	
181	504937	1.11.21	yes	no	6.11.21	77	m	66	13	5	
182	504008	1.11.21	no	no	6.11.21	60	m	76	16.4	5	
183	504671	2.11.21	no	no	8.11.21	54	m	66	14.5	6	
184	502356	3.11.21	yes	no	9.11.21	75	m	55	12.5	6	
185	505257	5.11.21	yes	no	10.11.21	54	m	63	14.5	5	
186	501383	5.11.21	no	yes	14.11.21	59	m	55	15	9	
187	504998	8.11.21	no	no	13.11.21	70	m	50	12.5	5	
188	477632	9.11.21	no	yes	18.11.21	56	m	43	15.7	9	
189	500527	10.11.21	yes	no	15.11.21	69	m	37	17.5	5	

190	504598	11.11.21	yes	no	16.11.21	49	m	53	17.8	5	
191	504213	11.11.21	no	yes	16.11.21	62	m	55	15	5	
192	505093	15.11.21	no	no	20.11.21	52	f	60	13	5	
193	504736	16.11.21	yes	no	22.11.21	59	m	68	15.5	6	
194	503451	16.11.21	no	no	21.11.21	47	m	40	14.6	5	
195	505150	17.11.21	yes	no	22.11.21	61	m	60	13.7	5	
196	505034	17.11.21	no	no	22.11.21	51	f	80	12.4	5	
197	504995	18.11.21	yes	no	23.11.21	72	m	60	13.8	5	
198	279274	18.11.21	no	yes	3.12.21	71	m	55	13.9	15	
199	483555	2.3.20	no	no	8.3.20	49	f	67	11.8	6	
200	482405	2.3.20	yes	no	8.3.20	44	m	65	8.6	6	
201	483951	3.3.20	no	no	9.3.20	67	m	58	8.9	6	
202	481430	3.3.20	yes	yes	10.3.20	58	m	42	11.9	7	
203	387037	3.3.20	no	no	8.3.20	68	m	51	10.5	5	
204	187410	4.3.20	yes	no	11.3.20	69	m	36	13.4	7	
205	483146	4.3.20	no	no	10.3.20	55	m	68	8.9	6	
206	481765	4.3.20	no	no	10.3.20	75	m	78	10.5	6	
207	483376	5.3.20	no	yes	11.3.20	38	m	53	8.5	6	
208	469481	5.3.20	no	yes	16.3.20	68	f	70	11.1	11	
209	483012	5.3.20	yes	no	10.3.20	44	m	56	9.9	5	
210	482342	6.3.20	yes	no	11.3.20	66	m	62	9.4	5	
211	482476	6.3.20	no	yes	12.3.20	64	m	47	10.5	6	
212	483289	6.3.20	no	no	11.3.20	61	m	69	10.5	5	
213	484410	10.3.20	no	no	15.3.20	57	m	57	10.6	5	
214	481716	10.3.20	no	no	15.3.20	80	m	55	10.9	5	
215	458872	10.3.20	yes	no	15.3.20	57	m	33	9.2	5	off pump
216	8900078	11.3.20	no	no	17.3.20	69	m	50	8.7	6	
217	479067	11.3.20	yes	no	16.3.20	59	m	63	11.1	5	off pump
218	481601	12.3.20	yes	no	18.3.20	59	f	33	10.1	6	
219	483676	12.3.20	no	yes	18.3.20	53	m	64	10.8	6	
220	238926	12.3.20	no	yes	18.3.20	65	m	59	9.5	6	
221	483103	13.3.20	yes	no	19.3.20	49	m	34	9	6	
222	484020	15.4.20	no	no	23.4.20	68	m	64	9.9	8	
223	484591	16.4.20	yes	no	24.4.20	69	m	73	11.1	8	
224	484554	20.4.20	no	no	28.4.20	58	m	64	9.3	8	
225	484920	20.4.20	yes	no	22.4.20	80	m	30	8	2	death
226	484894	21.4.20	yes	no	27.4.20	60	m	66	9.1	6	
227	484571	22.4.20	no	yes	30.4.20	67	m	65	10.3	8	
228	484475	23.4.20	no	no	1.5.20	40	m	62	12.7	8	
229	483583	27.4.20	no	no	4.5.20	77	m	62	8.6	7	
230	391596	27.4.20	no	no	5.5.20	65	m	70	15.5	8	
231	484647	28.4.20	yes	no	4.5.20	73	m	52	13.2	6	off pump
232	481142	29.4.20	no	no	4.5.20	72	m	62	14.4	5	
233	484484	30.4.20	no	no	8.5.20	64	f	71	11.3	8	
234	484761	4.5.20	yes	no	14.5.20	65	m	78	9.5	10	
235	484974	4.5.20	no	no	11.5.20	52	m	53	10.2	7	
236	483938	5.5.20	no	yes	11.5.20	57	m	54	12.8	6	
237	452107	5.5.20	no	no	12.5.20	64	f	75	11.1	7	
238	484771	6.5.20	yes	yes	12.5.20	69	m	54	10.2	6	
239	484437	8.5.20	no	no	13.5.20	55	m	46	9.8	5	

240	485003	11.5.20	yes	no	19.5.20	54	f	70	11.7	8	
241	484313	11.5.20	no	yes	17.5.20	61	m	73	9.9	6	
242	480718	12.5.20	no	no	21.5.20	56	m	63	10.7	9	
243	483996	13.5.20	yes	no	24.5.20	63	m	60	9.2	11	
244	485273	18.5.20	no	no	23.5.20	47	m	53	10.9	5	
245	485057	18.5.20	yes	no	23.5.20	54	m	68	11	5	
246	484691	19.5.20	no	yes	27.5.20	67	m	52	10.1	8	
247	481422	20.5.20	no	no	27.5.20	54	m	42	9.5	7	
248	483500	25.5.20	no	no	30.5.20	63	m	76	11.8	5	
249	485307	26.5.20	yes	no	1.6.20	72	m	76	13.7	6	
250	415737	27.5.20	no	no	1.6.20	55	m	51	11.8	5	
251	484623	28.5.20	yes	no	3.6.20	65	f	53	10.8	6	off pump
252	485386	28.5.20	no	no	2.6.20	61	m	60	10.8	5	
253	482468	29.5.20	no	no	4.6.20	44	m	80	10.1	6	
254	485391	1.6.20	yes	no	7.6.20	73	m	40	10.4	6	
255	252409	2.6.20	no	no	7.6.20	57	m	76	10.4	5	
256	485310	2.6.20	no	no	10.6.20	61	m	76	12.9	8	
257	479517	3.6.20	yes	no	8.6.20	53	m	65	9	5	
258	485509	4.6.20	yes	no	9.6.20	71	m	29	13.6	5	
259	460485	4.6.20	no	no	10.6.20	59	m	60	15.2	6	
260	485463	5.6.20	no	yes	17.6.20	72	m	58	11.7	12	
261	485369	5.6.20	yes	no	12.6.20	62	m	55	11.9	7	
262	485599	8.6.20	no	no	14.6.20	65	m	61	12.2	6	
263	206693	9.6.20	no	yes	15.6.20	72	m	56	15.6	6	
264	441478	10.6.20	no	no	19.6.20	50	m	28	13.2	9	
265	485164	12.6.20	no	no	18.6.20	56	m	52	9.1	6	
266	485465	12.6.20	yes	yes	21.6.20	69	m	46	10.5	9	
267	485373	15.6.20	yes	no	22.6.20	53	m	55	10.6	7	
268	221936	16.6.20	no	no	21.6.20	64	m	51	13.9	5	
269	484856	16.6.20	no	no	22.6.20	64	m	61	10.9	6	
270	485710	17.6.20	yes	no	22.6.20	43	m	58	10.5	5	
271	485296	17.6.20	no	no	23.6.20	63	m	56	11.3	6	
272	482484	17.6.20	no	no	27.6.20	70	m	66	10	10	
273	485815	19.6.20	yes	yes	26.6.20	63	m	82	10.2	7	
274	485878	19.6.20	no	no	24.6.20	61	m	50	9.9	5	
275	485944	20.6.20	no	no	3.7.20	64	m	48	13.8	13	
276	298676	22.6.20	yes	no	27.6.20	70	m	34	15.1	5	
277	472996	22.6.20	no	no	29.6.20	55	m	55	9	7	
278	485888	23.6.20	no	no	28.6.20	42	m	63	13.5	5	
279	485708	24.6.20	yes	no	29.6.20	53	m	56	14	5	
280	485973	24.6.20	no	no	30.6.20	62	f	60	13.2	6	
281	485862	25.6.20	yes	no	2.7.20	54	m	68	13	7	
282	485957	26.6.20	yes	no	4.7.20	59	m	57	14.1	8	
283	485787	29.6.20	no	no	4.7.20	64	m	61	14.9	5	
284	485663	30.6.20	yes	no	5.7.20	56	m	68	13.3	5	
285	486044	1.7.20	yes	no	8.7.20	50	m	76	14	7	
286	485379	1.7.20	no	no	6.7.20	45	m	52	13.6	5	
287	486148	3.7.20	no	no	10.7.20	67	m	37	13	7	
288	486106	6.7.20	yes	no	11.7.20	68	m	66	12	5	off pump
289	485664	7.7.20	yes	no	14.7.20	47	m	65	10	7	

290	486121	7.7.21	no	no	13.7.20	53	m	70	15.8	6	
291	340365	8.7.20	no	no	13.7.20	52	m	38	16.1	5	
292	486185	10.7.20	yes	no	23.7.20	63	m	49	13.6		death
293	467002	13.7.20	no	no	20.7.20	43	m	41	9.3	7	
294	486201	14.7.20	no	no	21.7.20	61	m	65	12.9	7	
295	485636	14.7.20	yes	no	21.7.20	66	m	51	15	7	
296	462692	15.7.20	no	no	28.7.20	55	f	29	9.5	13	
297	484876	15.7.20	yes	yes	8.8.20	65	m	67	15.7	24	
298	481751	16.7.20	no	no	29.7.20	52	m	44	13.7	13	
299	486086	17.7.20	yes	no	25.7.20	54	m	43	14.6	8	
300	486269	22.7.20	yes	no	29.7.20	57	m	65	14.1	7	
301	283006	23.7.20	no	yes	8.8.20	58	m	67	14.1	16	
302	477096	27.7.20	no	no	8.8.20	61	m	65	14.5	12	
303	486237	28.7.20	yes	no	8.8.20	65	m	42	13.3	11	
304	486452	10.8.20	no	no	17.8.20	52	m	70	13.6	7	
305	486564	11.8.20	yes	no	18.8.20	57	m	56	13.5	7	
306	486553	12.8.20	no	no	21.8.20	57	m	70	15.1	9	
307	485459	13.8.20	yes	no	22.8.20	59	m	57	14.8	9	
308	486432	14.8.20	no	no	11.9.20	57	m	30	14.2	28	
309	486969	17.8.20	no	no	24.8.20	45	m	57	14.2	7	
310	486736	18.8.20	no	yes	29.8.20	62	m	78	13.6	11	
311	486751	18.8.20	yes	no	27.8.20	81	m	69	12.1	9	
312	486647	18.8.20	yes	yes	26.8.20	68	m	80	15.1	8	
313	487289	20.8.20	no	no	28.8.20	59	f	38	9.8	8	
314	486659	19.8.20	no	no	26.8.20	58	m	67	16.8	7	
315	486847	21.8.20	no	no	3.10.20	45	m	76	16.1	43	
316	484037	21.8.20	yes	no	28.8.20	57	f	62	13.9	7	
317	487035	24.8.20	yes	no	29.8.20	60	m	68	14.3	5	
318	359124	25.8.20	yes	no	2.9.20	56	m	66	14.7	8	
319	487433	27.8.20	no	yes	14.10.20	65	f	59	10.5	18	death
320	486901	3.9.20	yes	no	10.9.20	52	m	60	14.8	7	off pump
321	487234	3.9.20	no	no	10.9.20	77	m	57	14	7	
322	486014	4.9.20	no	no	11.9.20	55	f	55	11.4	7	
323	487547	4.9.20	no	no	11.9.20	54	m	69	14.9	7	
324	464653	7.9.20	no	no	14.9.20	71	m	74	11.3	7	
325	486548	7.9.20	yes	no	14.9.20	62	f	54	11.9	7	
326	486105	8.9.20	no	no	15.9.20	42	m	76	13.2	7	
327	486122	8.9.20	no	no	15.9.20	73	m	65	10.4	7	
328	462250	9.9.20	yes	no	16.9.20	46	m	70	16	7	
329	487213	9.9.20	no	no	16.9.20	66	m	75	15.5	7	
330	487497	11.9.20	yes	no	18.9.20	76	m	62	12.6	7	off pump
331	487357	11.9.20	no	yes	18.9.20	65	f	73	12.1	7	
332	486680	13.9.20	yes	yes	20.9.20	72	m	41	16	7	
333	487306	14.9.20	yes	no	21.9.20	48	m	72	16.8	7	off pump
334	487261	14.9.20	no	no	21.9.20	68	m	67	13.4	7	
335	486229	15.9.20	yes	no	22.9.20	69	m	66	10.8	7	off pump
336	487301	15.9.20	no	yes	21.10.21	64	f	69	12.2	36	
337	487533	16.9.20	no	no	23.9.20	60	m	58	14.1	7	
338	487635	17.9.20	yes	no	25.9.20	53	m	37	15.2	8	
339	487408	18.9.20	no	yes	25.9.20	40	m	57	14.4	7	

340	486686	21.9.20	no	yes	28.9.20	50	m	58	15.8	7	
341	487877	21.9.20	yes	no	28.9.20	54	m	72	15.8	7	
342	487673	22.9.20	yes	yes	30.9.20	52	m	62	15.6	8	
343	487756	23.9.20	no	yes	30.9.30	67	m	62	14.6	7	
344	487930	24.9.20	yes	no	1.10.20	65	m	52	14.6	7	
345	487751	25.9.20	yes	no	2.10.20	56	m	60	13.8	7	
346	488186	25.9.20	no	yes	28.9.20	67	m	65	9.7	3	death
347	487596	28.9.20	no	no	5.10.20	61	m	75	16.2	7	
348	487780	28.9.20	no	no	8.10.20	64	m	60	13.3	10	
349	488065	29.9.20	yes	no	6.10.20	59	m	57	13.5	7	
350	487753	30.9.20	yes	no	7.10.20	63	m	76	16.4	7	
351	342583	1.10.20	no	yes	17.10.20	46	m	58	14.9	16	
352	487996	5.10.20	yes	no	13.10.20	55	m	70	12.7	8	
353	487969	7.10.20	no	yes	17.10.20	65	f	75	10.1	10	
354	488282	12.10.20	no	no	19.10.20	55	m	71	14.1	7	
355	488701	13.10.20	yes	no	20.10.20	66	f	75	11.5	7	
356	488106	13.10.20	no	no	20.10.20	55	m	68	13	7	
357	486119	15.10.20	yes	yes	22.10.20	60	m	59	10.5	7	
358	488384	19.10.20	yes	no	29.10.20	42	m	47	14.1	10	
359	488671	19.10.21	no	no	29.10.20	49	m	82	14.7	10	
360	488306	20.10.20	yes	no	29.10.20	64	m	70	14.9	9	
361	488407	20.10.20	no	no	29.10.20	72	m	37	13.7	9	
362	488851	21.10.20	no	no	29.10.20	53	m	55	14	8	
363	488766	5.11.20	no	no	12.11.20	50	f	42	13.4	7	
364	488515	6.11.20	yes	yes	16.11.20	57	f	61	12.6	10	
365	489582	6.11.20	no	no	13.11.20	55	f	55	14	7	
366	488967	9.11.20	no	no	16.11.20	72	m	60	12.3	7	
367	488113	9.11.20	no	no	16.11.20	55	m	55	15.6	7	
368	488325	10.11.20	no	yes	17.11.20	72	m	49	14.9	7	
369	488496	10.11.20	yes	no	17.11.20	47	m	64	14	7	
370	489431	11.11.20	yes	no	18.11.20	78	m	68	14.1	7	
371	488749	11.11.20	no	no	17.11.20	69	m	71	13	6	
372	483613	12.11.20	no	no	20.11.20	51	m	42	15.2	8	
373	487917	12.11.20	no	no	19.11.20	63	m	58	16.2	7	
374	300588	13.11.20	yes	no	20.11.20	60	m	23	14.1	7	
375	489753	16.11.20	yes	no	23.11.20	78	m	47	12.3	7	
376	489899	16.11.20	no	no	25.11.20	67	m	40	12.9	9	
377	487676	18.11.20	no	no	25.11.20	55	m	39	14	7	
378	489904	19.11.20	yes	no	26.11.20	45	m	72	14.6	7	off pump
379	488934	20.11.20	no	no	27.11.20	61	m	54	16.1	7	
380	489635	24.11.20	yes	no	1.12.20	67	m	73	14	7	
381	489226	25.11.20	no	yes	7.12.20	73	m	43	14.7	12	
382	490188	1.12.20	no	no	10.12.20	53	m	39	15.3	9	
383	489792	3.12.20	yes	no	3.2.21	60	m	64	12.4	62	
384	490458	7.12.20	yes	no	14.12.20	59	m	48	11.8	7	
385	490333	7.12.20	no	no	14.12.20	57	m	73	14.2	7	
386	490323	8.12.20	no	no	14.12.20	57	m	58	14.8	6	
387	488887	8.12.20	yes	no	14.12.20	47	m	55	11.1	6	
388	490568	9.12.20	yes	no	16.12.20	55	m	59	9.3	7	
389	490231	9.12.20	no	no	16.12.20	51	m	20	10.3	7	

390	489258	10.12.20	yes	no	17.12.20	51	m	65	15.3	7	
391	490320	11.12.20	no	no	28.12.20	56	m	65	15.3	17	
392	491003	14.12.20	yes	no	23.12.20	72	m	43	9.7	9	
393	489335	14.12.20	no	no	21.12.20	65	m	62	13.6	7	
394	488389	14.12.20	no	yes	21.12.20	68	m	55	12.3	7	
395	489958	15.12.20	yes	no	21.12.20	58	m	34	10.2	6	
396	486645	16.12.20	yes	no	21.12.20	60	m	54	14.5	5	
397	490463	16.12.20	no	yes	26.12.20	60	m	44	13.9	10	
398	485404	17.12.20	yes	no	22.12.20	66	m	78	12.8	5	
399	490196	17.12.20	no	yes	31.12.20	52	f	56	14.4	14	
400	491038	21.12.20	yes	yes	29.12.20	67	m	78	14.8	8	
401	490782	22.12.20	yes	no	28.12.20	65	m	63	13.4	6	
402	489261	23.12.20	yes	no	28.12.20	57	m	66	15	5	
403	487929	23.12.20	no	yes	29.12.20	66	m	44	14.4	6	
404	489085	23.12.20	no	no	30.12.20	51	m	63	11.8	7	
405	490777	24.12.20	yes	no	29.12.20	53	m	76	14.8	5	
406	484614	28.12.20	yes	yes	3.1.21	68	f	65	11.4	6	off pump
407	489783	29.12.20	yes	no	3.1.21	50	m	70	12.8	5	off pump
408	490853	29.12.20	no	no	3.1.21	56	m	80	13.8	5	
409	491044	30.12.20	no	no	5.1.21	44	m	29	15	6	
410	491683	30.12.20	yes	no	5.1.21	46	m	60	14.2	6	
411	278607	31.12.20	yes	no	5.1.21	48	m	80	11.6	5	
412	491037	31.12.20	no	no	6.1.21	69	m	76	13.5	6	
413	491291	4.1.21	yes	no	11.1.21	67	m	66	11.4	7	
414	491733	4.1.21	no	no	12.1.21	77	m	66	11	8	
415	489780	5.1.21	no	no	11.1.21	55	m	64	10.2	6	
416	491239	5.1.21	yes	no	11.1.21	56	m	58	16	6	
417	487652	6.1.21	no	no	12.1.21	68	m	70	11.6	6	
418	491563	6.1.21	no	no	13.1.21	63	m	53	14.2	7	
419	492154	7.1.21	no	no	13.1.21	67	m	50	14.6	6	
420	491173	7.1.21	no	no	13.1.21	55	m	47	14.4	6	
421	491178	8.1.21	no	no	14.1.21	43	m	43	13.1	6	
422	491168	8.1.21	no	no	15.1.21	61	m	59	14.3	7	
423	490501	11.1.21	yes	no	18.1.21	58	m	48	13.7	7	
424	490465	11.1.21	no	yes	18.1.21	66	f	69	12	7	
425	491345	12.1.21	no	yes	22.1.21	69	f	71	12.6	10	
426	491474	12.1.21	yes	no	20.1.21	59	m	59	13.9	8	
427	492002	12.1.21	no	no	17.1.21	60	m	58	14.4	5	
428	491482	13.1.21	yes	yes	23.1.21	63	f	63	12	10	
429	491229	13.1.21	no	no	18.1.21	48	f	72	14.1	5	
430	488845	14.1.21	no	no	19.1.21	64	m	66	13.2	5	off pump
431	491748	14.1.21	yes	no	22.1.21	61	m	66	13.7	8	
432	492210	15.1.21	no	no	20.1.21	63	m	75	14.3	5	
433	491673	15.1.21	no	no	20.1.21	54	m	68	15.7	5	
434	492669	18.1.21	yes	no	23.1.21	71	m	55	12.4	5	
435	491884	18.1.21	no	yes	25.1.21	53	m	55	11	7	
436	487982	19.1.21	no	no	24.1.21	65	m	49	14.7	5	
437	492151	19.1.21	yes	no	24.1.21	54	m	52	8.6	5	
438	491233	20.1.21	no	no	27.1.21	64	m	59	13.8	7	
439	491487	20.1.21	yes	no	25.1.21	47	m	72	14.8	5	

440	492265	21.1.21	no	no	27.1.21	55	m	55	11.1	6	
441	492316	21.1.21	yes	no	29.1.21	56	m	58	15	8	
442	249987	22.1.21	yes	no	27.1.21	55	m	62	15.1	5	
443	492383	25.1.21	no	no	31.1.21	67	m	59	10.6	6	
444	489199	25.1.21	yes	no	31.1.21	44	m	45	14.9	6	off pump
445	492485	25.1.21	no	no	30.1.21	60	m	61	10.1	5	
446	492656	27.1.21	no	no	3.2.21	71	f	44	11.1	7	
447	492785	27.1.21	yes	no	2.2.21	57	m	73	10.6	6	
448	475032	27.1.21	no	no	3.2.21	54	m	68	16.6	7	
449	295399	28.1.21	yes	yes	9.2.21	68	m	48	16.5	12	
450	488083	28.1.21	no	no	5.2.21	61	m	44	14.9	8	
451	491940	29.1.21	yes	no	3.2.21	55	m	42	10.2	5	off pump
452	492089	29.1.21	no	no	4.2.21	60	m	55	11	6	
453	492858	1.2.21	yes	no	6.2.21	44	m	67	14.7	5	
454	492555	1.2.21	no	no	6.2.21	61	m	72	14.8	5	
455	485293	1.2.21	no	no	6.2.21	55	f	58	13	5	
456	491134	2.2.21	no	no	8.2.21	64	m	70	15.3	6	
457	492794	2.2.21	yes	no	9.2.21	50	m	60	16.4	7	
458	490875	3.2.21	no	no	3.2.21	68	f	40	12.8	0	death
459	492920	4.2.21	no	yes	11.2.21	67	m	34	10	7	
460	491727	5.2.21	yes	no	11.2.21	69	m	74	13	6	
461	491282	5.2.21	no	no	11.2.21	73	m	61	9.9	6	
462	492977	8.2.21	no	no	15.2.21	62	m	62	14.1	7	
463	493727	8.2.21	yes	yes	15.2.21	66	m	66	15.6	7	
464	493034	9.2.21	no	no	15.2.21	63	m	53	14.5	6	
465	354467	10.2.21	no	no	18.2.21	64	m	68	12.5	8	
466	318495	10.2.21	yes	no	15.2.21	55	m	41	12.8	5	off pump
467	493121	9.2.21	yes	yes	15.2.21	67	f	65	10.7	6	
468	493029	11.2.21	yes	no	19.2.21	51	m	55	16.1	8	
469	492789	12.2.21	yes	no	17.2.21	55	f	55	10.9	5	
470	493902	12.2.21	no	no	17.2.21	55	m	60	13.7	5	
471	493117	15.2.21	no	no	21.2.21	50	m	65	13.7	6	
472	490096	15.2.21	yes	no	21.2.21	56	m	58	17.2	6	
473	493348	16.2.21	yes	no	21.2.21	51	m	60	9	5	
474	493195	16.2.21	no	yes	27.2.21	67	m	55	12.4	11	
475	493114	17.2.21	no	no	24.2.21	60	m	40	13.6	7	
476	493191	18.2.21	no	no	25.2.21	58	f	68	13.3	7	
477	493491	18.2.21	yes	no	24.2.21	52	m	65	13.6	6	
478	493839	18.2.21	no	no	24.2.21	60	m	59	12.2	6	
479	493494	22.2.21	yes	no	1.3.21	54	m	45	15	7	
480	494200	22.2.21	no	no	27.2.21	68	m	70	16.1	5	
481	492856	23.2.21	yes	no	1.3.21	55	f	57	12.6	6	
482	197575	25.2.21	yes	no	2.3.21	55	f	57	15.7	5	
483	494256	26.2.21	no	no	4.3.21	52	f	72	9.3	6	
484	425236	1.3.21	no	yes	8.3.21	62	m	56	15.1	7	
485	494625	1.3.21	yes	no	7.3.21	59	m	58	13.9	6	
486	492065	3.3.21	yes	no	10.3.21	40	m	65	14.1	7	
487	493407	3.3.21	no	no	8.3.21	49	m	68	14.5	5	
488	494417	4.3.21	yes	yes	13.3.21	72	m	53	13.5	9	
489	494261	5.3.21	no	no	10.3.21	57	m	44	13.9	5	

490	494556	8.3.21	no	no	23.3.21	39	m	47	14.3	15	
491	493913	8.3.21	yes	no	14.3.21	46	m	35	10.7	6	
492	495117	9.3.21	yes	no	15.3.21	54	m	68	16.6	6	
493	491668	10.3.21	no	yes	22.3.21	60	m	33	14	12	
494	494465	10.3.21	yes	no	15.3.21	55	m	64	15.2	5	
495	493606	12.3.21	no	no	17.3.21	52	m	63	13.1	5	
496	9602821	12.3.21	yes	no	22.3.21	67	m	76	11.3	10	
497	361721	15.3.21	no	no	20.3.21	54	m	72	13.4	5	
498	494736	15.3.21	yes	no	21.3.21	57	m	64	14.6	6	
499	495151	16.3.21	yes	no	22.3.21	52	m	42	14.8	6	
500	494738	17.3.21	no	no	25.3.21	61	m	76	11.6	8	
501	495197	17.3.21	yes	no	23.3.21	52	m	38	14.7	6	
502	494620	18.3.21	no	no	23.3.21	55	m	74	14.3	5	
503	495047	22.3.21	no	no	27.3.21	37	m	46	15.5	5	
504	494866	22.3.21	no	no	31.3.21	69	f	70	11.5	9	
505	495967	23.3.21	yes	no	28.3.21	60	m	70	13.1	5	
506	495249	23.3.21	yes	no	28.3.21	37	m	47	16.8	5	
507	495471	25.3.21	yes	yes	30.3.21	62	m	60	15.6	5	
508	494714	25.3.21	no	no	30.3.21	63	f	80	12	5	
509	495263	26.3.21	yes	no	31.3.21	38	m	51	14.9	5	
510	493669	26.3.21	no	no	1.4.21	65	m	52	10.8	6	
511	495970	26.3.21	no	no	31.3.21	60	m	70	15.6	5	
512	496064	29.3.21	yes	no	5.4.21	41	m	65	14.9	7	
513	496696	27.3.21	no	yes	3.4.21	78	m	52	12	7	death
514	495623	29.3.21	no	no	5.4.21	48	m	47	16.1	7	
515	495112	30.3.21	yes	no	5.4.21	59	m	70	14.5	6	
516	260062	31.3.21	no	yes	8.4.21	59	m	54	12.2	8	
517	496086	31.3.21	no	no	5.4.21	65	m	62	12.7	5	