

OUTCOMES OF POST CLOSED MITRAL
VALVOTOMY MITRAL VALVE REPLACEMENT-
A RETROSPECTIVE COHORT STUDY



Thesis Submitted By

Dr. RENJITH S

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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
TRIVANDRUM, KERALA, INDIA – 695011

Declaration

I, **Dr Renjith S**, hereby declare that this thesis titled "*Outcomes of Post Closed Mitral Valvotomy Mitral Valve Replacement- A retrospective cohort study*" has been prepared by me under the capable supervision and guidance of **Prof.**

Jayakumar K, Professor and Head of the department and

Dr.Varghese.T.Panicker, Additional Professor, **Dr.Bineesh K.R**, Assistant Professor Department of Cardiothoracic and Vascular Surgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

Thiruvananthapuram

30-07-2018

Dr Renjith S

Senior Resident

Department of Cardio Vascular and Thoracic Surgery

SCTIMST

Certificate

We hereby certify that this thesis titled

“Outcomes of Post Closed Mitral Valvotomy Mitral Valve Replacement- A retrospective cohort study” is the bonafide work of **Dr Renjith S**, MCh CVTS resident, done under our guidance at Department of cardiovascular and thoracic surgery at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

He has shown keen interest in preparing this project.

Prof. Jayakumar K

Senior Professor and Head of the Department
Department of Cardiovascular and Thoracic Surgery
SCTIMST, Thiruvananthapuram

Dr. Varghese T Panicker

Additional Professor
Department of Cardiovascular and Thoracic Surgery
SCTIMST, Thiruvananthapuram

Dr. Bineesh K R

Assistant Professor
Department of Cardiovascular and Thoracic Surgery
SCTIMST, Thiruvananthapuram

Certificate

I hereby certify that this thesis titled

*“Outcomes of Post Closed Mitral Valvotomy Mitral Valve Replacement- A
retrospective cohort study”*

Is the bonafide record of work done by **Dr Renjith S**, MCh CVTS resident, done
at Department of Cardiovascular and Thoracic surgery at Sree Chitra Tirunal
Institute for Medical Sciences & Technology, Thiruvananthapuram.

Prof. Jayakumar K

Senior Professor and Head of the Department
Department of Cardiovascular and Thoracic Surgery
SCTIMST, Thiruvananthapuram

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30-07-2018

Thiruvananthapuram

Dr Renjith S

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ABBREVIATIONS AND EXPANSIONS

MV MITRAL VALVE

MS MITRAL STENOSIS

MVR MITRAL VALVE REPLACEMENT

CMC CLOSED MITRAL COMMISSUROTOMY

CMV CLOSED MITRAL VALVOTOMY

OMV OPEN MITRAL VALVOTOMY

BMV BALLOON MITRAL VALVOTOMY

RV RIGHT VENTRICLE

PAH PULMONARY ARTERIAL HYPERTENSION

RVSP RIGHT VENTRICULAR SYSTOLIC PRESSURE

CPB CARDIOPULMONARY BYPASS

TR TRICUSPID REGURGITATION

MR MITRAL REGURGITATION

BSA BODY SURFACE AREA

TITLE

**Outcomes of Post Closed
Mitral Valvotomy Mitral Valve
Replacement- A retrospective
cohort study**

INTRODUCTION

INTRODUCTION

Mitral stenosis in the younger age group is a unique condition and a great majority of these patients rapidly develop significant pulmonary hypertension and congestive cardiac failure. The first successful closed mitral commissurotomy was reported as early as 1923 by Cutler and Levine and this was followed by a report by Souttar in 1925 [1]. Three decades later this procedure was resurrected by Harken [2], Bailey, and Baker *et al.* Closed mitral commissurotomy (CMC) was the first effective intervention in valvular heart disease which provides excellent long-term hemodynamic and clinical improvement.

Rheumatic mitral valvular heart disease is common in developing countries although its incidence is decreasing in western countries. Closed mitral commissurotomy (CMC) was the first effective intervention in valvular heart disease which provides excellent long-term hemodynamic and clinical improvement. It has been shown that when symptomatic deterioration occurs late after CMC, mitral valve replacement (MVR) restores clinical and hemodynamic improvement in many patients. Mitral re-stenosis is the most frequent cause of reoperation. Because of the severity of the valve disease in most of these patients, mitral valve replacement is usually performed [3].

AIM OF THE STUDY

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Primary objective- To compare the immediate and early postoperative outcomes of Mitral Valve Replacement in patients with and without history of Closed mitral valvotomy

Secondary objective- To study the changes in Right Ventricular Function and Pulmonary artery hypertension in patients with history of closed mitral valvotomy undergoing Mitral Valve Replacement

REVIEW OF LITERATURE

Review of literature

Evolution of mitral valve surgery

The surgical treatment of mitral stenosis by relief of the mechanical obstruction was first suggested by Sir Lauder Brunton of London Hospital in 1902 [4]. He suggested in Lancet that it might be satisfactory to merely open up the stenosed mitral valve mechanically with a knife. As is often the case with new ideas that go against the grain of accepted thinking, his idea was solidly rebuked by an editorial in the very next issue of Lancet [5]. Nevertheless, Brunton's suggestion triggered an awakening to the possibility of surgical treatment of valvular heart disease, and during the period 1902 to 1923 there were a number of experimental reports published on the creation and relief of mitral stenosis [6-10].

In 1923 Elliot Carr Cutler, in conjunction with his cardiology colleague, Samuel Levine, performed a closed transventricular mitral commissurotomy with a neurosurgical tenotomy knife, as the cardiac valvulotome had not yet been completed, on a 12-year-old patient dying of rheumatic mitral stenosis at the Peter Bent Brigham Hospital [11]. This operation was carried out after several years of experimentation regarding resuscitation of the heart, appropriate incisions, and the pathophysiology of mitral stenosis. The interest in mitral stenosis was rampant at the time because of the huge number of patients suffering from this public health problem. The patient survived and went on to die of pneumonia 4 years postoperatively. Subsequent to this, Cutler performed seven more operations using his new cardiovalvulotome [figure: 1], which was to create controlled mitral regurgitation. Unfortunately, once the cardiac valvulotome was completed and in use in the operating room, the severe mitral regurgitation it caused resulted in the death of the next seven patients Cutler operated upon. In 1929, at the

American Surgical Association meeting, Cutler announced that he was declaring a moratorium on this operation due to its high mortality [11].

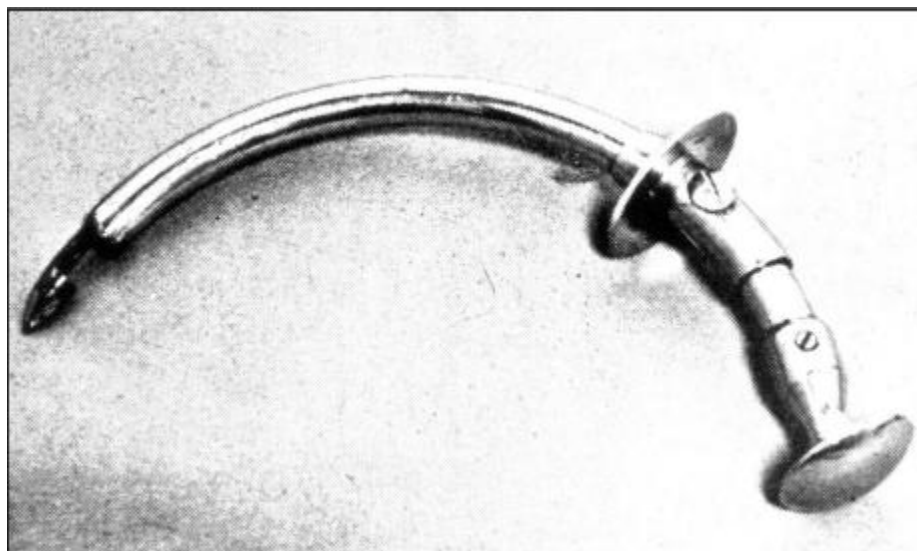


Figure 1: Cardiac valvulotome

Interestingly, in 1925, British surgeon Henry Souttar had performed what is now considered to be the first finger-fracture valvuloplasty for mitral stenosis through the left atrial appendage via a left thoracotomy [1]. This was an operation that would become relatively standard over the next 20 years, despite the fact that London physicians of the era disapproved of Souttar's approach and did not refer him another patient upon which to operate.

Mitral valve surgery was not revived until after World War II, with the pioneering work of another Brigham surgeon, Dr Dwight Harken [2], and that of Dr Charles Bailey [15] in Philadelphia, who did the first large-scale surgical treatment of mitral valve disease by valvuloplasty. In a landmark paper in 1948, Harken was one of the first to show that the surgical treatment of mitral stenosis could be performed safely and reproducibly by closed techniques

[2]. Interestingly, he originally started out using the cardiac valvulotome, but quickly realized that the resultant mitral regurgitation was too severe and switched to the finger-fracture technique of Souttar. He then commenced a very large and long series of closed mitral valvuloplasties for mitral stenosis that were remarkably successful. His landmark studies with Lawrence Ellis, another Brigham cardiologist, were important for several reasons. They showed that closed mitral valvuloplasty could be successfully done in a large number of patients, but more importantly, they were some of the first studies to show in a rather preliminary way actuarial results of cardiac operations. In 1973, Harken and Ellis presented a 20- year follow-up of 710 patients showing mortality and re-operation rates, measures which became standard for cardiac surgery outcomes studies [16].

After the development of cardiopulmonary bypass, open mitral valvotomy was performed under direct vision for mitral stenosis in 1956 with improved hemodynamic results [17-22]. Till recently, in developed countries, closed mitral commissurotomy was still preferred to the open technique [23], with an ongoing controversy about the best approach [19-21, 24].

Rheumatic heart disease and mitral valve disease

Rheumatic heart disease remains a major cause of morbidity and mortality in children and young adults in the developing world with a peak age group of 25 to 35 years [25-27].

Rheumatic heart disease affects the mitral valve in up to 50% of cases [28,29] and results in mitral insufficiency, mitral stenosis, or both. In young patients, mitral regurgitation is predominant, but mitral stenosis becomes progressively more common with age.[25,30,31]

Regurgitant rheumatic valves are edematous with fibrous thickening and minimal calcification, nonfused commissures, annular dilatation, and anterior chordal elongation, whereas stenotic rheumatic valves have stiff and restricted leaflets, commissural fusion, annular calcification, and chordal fusion[32-35].

Other conditions which may cause mitral stenosis (MS) include congenital disease, mitral annular calcification, rheumatoid arthritis, SLE and carcinoid syndrome.

Non-rheumatic mitral stenosis

Mitral annular calcification is a chronic degenerative condition of the fibrous mitral annulus, resulting in progressive calcification, particularly involving the posterior annulus [36]. The estimated prevalence of mitral annular calcification is 10% of elderly patients, with 1–2% of whom develop stenosis [36-38]. Risk factors for mitral annular calcification include older age, being a woman, having chronic kidney disease, and diseases predisposing to left ventricular hypertrophy (ie, hypertension and aortic stenosis) [39]. Mitral annular calcification seems to be a multifactorial condition resulting from a varying combination of abnormal calcium and

phosphorus metabolism,[40] increased mitral valve haemodynamic stress,[42]and atherosclerotic processes [42–44].

Natural history of mitral stenosis and presentation

The normal mitral orifice is 4–5 cm² in area and symptoms do not occur until the orifice area falls to below 2.0 cm² and usually below 1.5 cm². The orifice area decreases by 0.1–0.3 cm² per year [45,46]. In one study, symptoms developed 16 years after the acute illness and become severe after a further 9 years [47]. The 5 year survival with severe symptomatic MS was 44% without surgery. The restricted mitral valve orifice area leads to elevated left atrial pressure which in turn increases pulmonary venous pressure causing exertional dyspnoea. Chronic pulmonary hypertension eventually ensues with the development of right-sided heart failure. Pulmonary pressures are raised in MS initially by passive back-pressure and reactive vasoconstriction. Ultimately histological changes occur similar to those seen in primary pulmonary hypertension and these may be irreversible [48]. The left ventricle is protected since it is downstream from the valve lesion. However, the right ventricle is under threat as pulmonary artery pressure rises. Established right heart failure as a result of pulmonary hypertension may cause a reduction in breathlessness as a result of lowered left atrial filling pressures. However, this apparent improvement is spurious and a sign of end-stage and usually inoperable disease.

Severity of MS

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
A	At risk of MS	<ul style="list-style-type: none"> Mild valve doming during diastole 	<ul style="list-style-type: none"> Normal transmitral flow velocity 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> None
B	Progressive MS	<ul style="list-style-type: none"> Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets Planimetered MVA >1.5 cm² 	<ul style="list-style-type: none"> Increased transmitral flow velocities MVA >1.5 cm² Diastolic pressure half-time <150 ms 	<ul style="list-style-type: none"> Mild-to-moderate LA enlargement Normal pulmonary pressure at rest 	<ul style="list-style-type: none"> None
C	Asymptomatic severe MS	<ul style="list-style-type: none"> Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets Planimetered MVA ≤1.5 cm² (MVA ≤1.0 cm² with very severe MS) 	<ul style="list-style-type: none"> MVA ≤1.5 cm² (MVA ≤1.0 cm² with very severe MS) Diastolic pressure half-time ≥150 ms (Diastolic pressure half-time ≥220 ms with very severe MS) 	<ul style="list-style-type: none"> Severe LA enlargement Elevated PASP >30 mmHg 	<ul style="list-style-type: none"> None
D	Symptomatic severe MS	<ul style="list-style-type: none"> Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets Planimetered MVA ≤1.5 cm² 	<ul style="list-style-type: none"> MVA ≤1.5 cm² (MVA ≤1.0 cm² with very severe MS) Diastolic pressure half-time ≥150 ms (Diastolic pressure half-time ≥220 ms with very severe MS) 	<ul style="list-style-type: none"> Severe LA enlargement Elevated PASP >30 mmHg 	<ul style="list-style-type: none"> Decreased exercise tolerance Exertional dyspnea

The transmitral mean pressure gradient should be obtained to further determine the hemodynamic effect of the MS and is usually >5 mmHg to 10 mmHg in severe MS; however, due to the variability of the mean pressure gradient with heart rate and forward flow, it has not been included in the criteria for severity.

LA indicates left atrial; LV, left ventricular; MS, mitral stenosis; MVA, mitral valve area; and PASP, pulmonary artery systolic pressure.

Figure 2: Severity of MS : 2014 AHA/ACC Valvular Heart Disease Guideline [49]

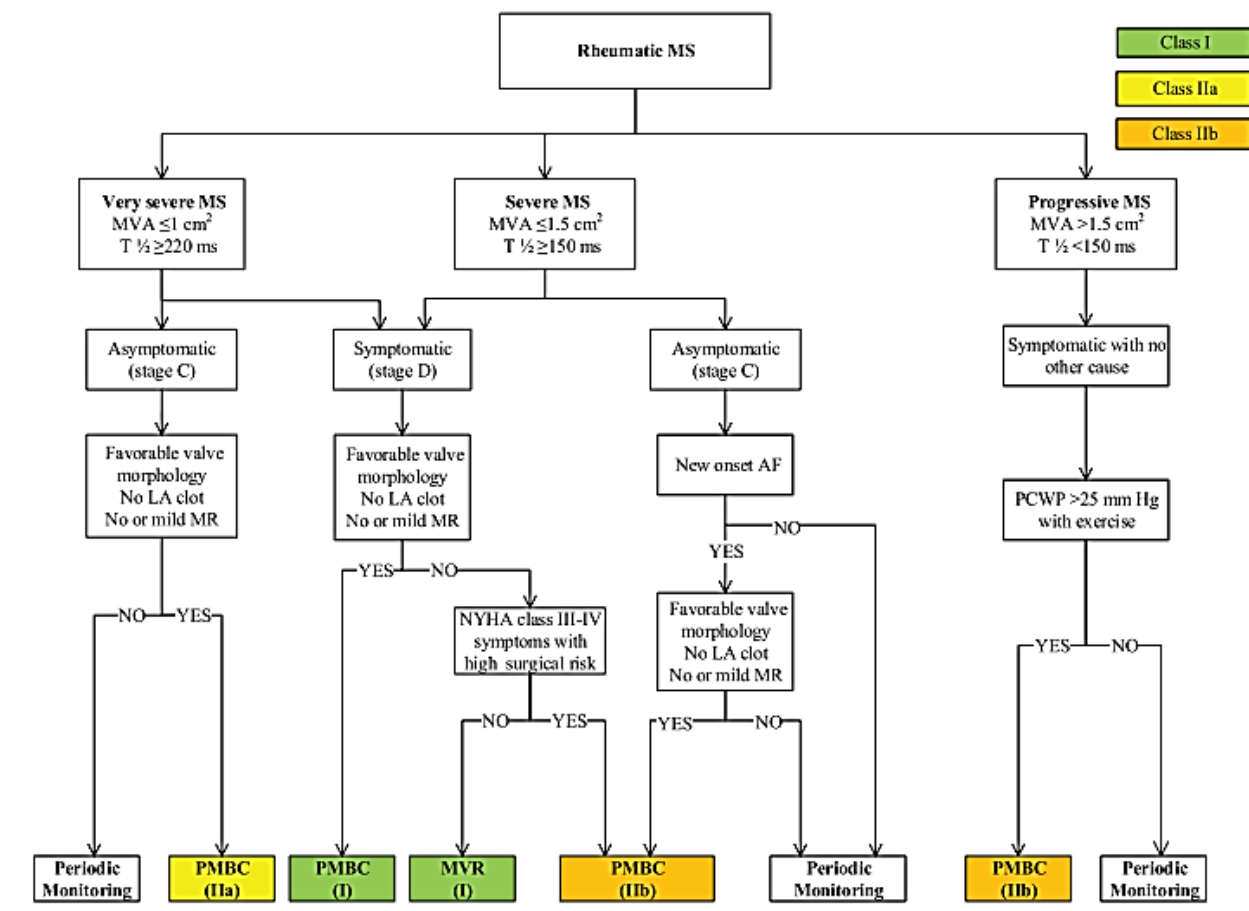


Figure 3: Indications for Intervention for Rheumatic MS [49]

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY DESIGN

Single center retrospective cohort study.

POPULATION

Patients who underwent mitral valve replacement (MVR) between 2008 and 2012

INCLUSION CRITERIA

All patients who underwent mitral valve replacement between 2008 and 2012 with a previous history of closed mitral valvotomy were taken as exposed group (cohort 1) and those who underwent mitral valve replacement without history of closed mitral valvotomy were taken into the unexposed group (cohort 2).

EXCLUSION CRITERIA

- Patients with history of balloon mitral valvotomy, open mitral commissurotomy were not included.
- Patients who underwent redo MVR were excluded.
- Patients who underwent other cardiac surgeries along with MVR were also excluded.

APPROVAL FROM TECHNICAL ADVISORY COMMITTEE (TAC):

TAC approval was obtained before commencing the study.

APPROVAL FROM INSTITUTIONAL ETHICS COMMITTEE (IEC):

IEC approval was taken before commencing the study.

METHODOLOGY

Patients who satisfied the inclusion criteria were included in the study. Data was collected with a semi structured questionnaire from hospital records and analysed. Pre-operative details, immediate post surgery echocardiography parameters, follow up echocardiography details at 1year and 5 years were collected from hospital records. Data was analysed after consultation with the statistician.

DATA COLLECTED

Following data was collected from case records.

1. AGE
2. SEX
3. HEIGHT
4. WEIGHT
5. BSA

6. COMORBIDITIES
 - a) DIABETES MELLITUS (DM)
 - b) HYPERTENSION (HTN)
 - c) OTHERS

8. DURATION OF DISEASE
9. TIME PERIOD BETWEEN ONSET OF DISEASE AND CMV

10. TIME PERIOD BETWEEN CMV AND MVR

PREOPERATIVE DETAILS

11. FUNCTIONAL CLASS

12. PREOPERATIVE RHYTHM

13. PREOPERATIVE ECHOCARDIOGRAPHY

- a) EJECTION FRACTION (EF)
- b) MITRAL STENOSIS GRADIENT
- c) MR
- d) LA
- e) AORTA
- f) TR
- g) RVSP
- h) RV FUNCTION

INTRAOPERATIVE DETAILS

14. CARDIOPULMONARY BYPASS TIME

15. AORTIC CROSS CLAMP TIME

16. VALVE SIZE

17. SUBVALVULAR PATHOLOGY

POSTOPERATIVE DETAILS

18. HOURS OF VENTILLATION

19. DAYS IN ICU

20. NUMBER OF DAYS OF HOSPITAL STAY

21. IONOTROPIC SCORE

22. RHYTHM

23. POST OPERATIVE ECHOCARDIOGRAPHY

IMMEDIATE

1 YEAR

5 YEAR

- a) MS GRADIENT
- b) MR
- c) EF
- d) RVFUNCTION (TAPSE)
- e) TR
- f) PAH
- g) LA
- h) AORTA

OUTCOME PARAMETERS:

1. Persistent Pulmonary hypertension - PH was diagnosed if systolic pulmonary artery pressure (sPAP) estimated by Doppler echocardiography was >40 mmHg.
2. Right ventricular dysfunction defined by either right ventricular end-diastolic diameter > 30 mm, right ventricular/left ventricular end-diastolic diameter > 1 or right ventricular hypokinesia or TAPSE as defined as the total excursion of the tricuspid annulus from tele-diastole to end-systole less than 16 or dilation of the RV (> 2/3 of the LV in its transversal diameter) Other criteria included paradoxical septal wall motion, pulmonary hypertension and severe tricuspid regurgitation.

CALCULATED PARAMETERS

Following parameters were calculated using collected data.

- BODY SURFACE AREA**
- VASOACTIVE INOTROPIC SCORE-**

**_Wernowsky Inotropic Score = Dopamine dose ($\mu\text{g}/\text{kg}/\text{min}$) + Dobutamine dose ($\mu\text{g}/\text{kg}/\text{min}$) +100 \times epinephrine dose ($\mu\text{g}/\text{kg}/\text{min}$)
VIS = IS + 10 X Milrinone dose ($\mu\text{g}/\text{kg}/\text{min}$) +10,000 \times Vasopressin dose (U/kg/min)
+ 100 \times Norepinephrine dose ($\mu\text{g}/\text{kg}/\text{min}$)**

STATISTICAL ANALYSIS

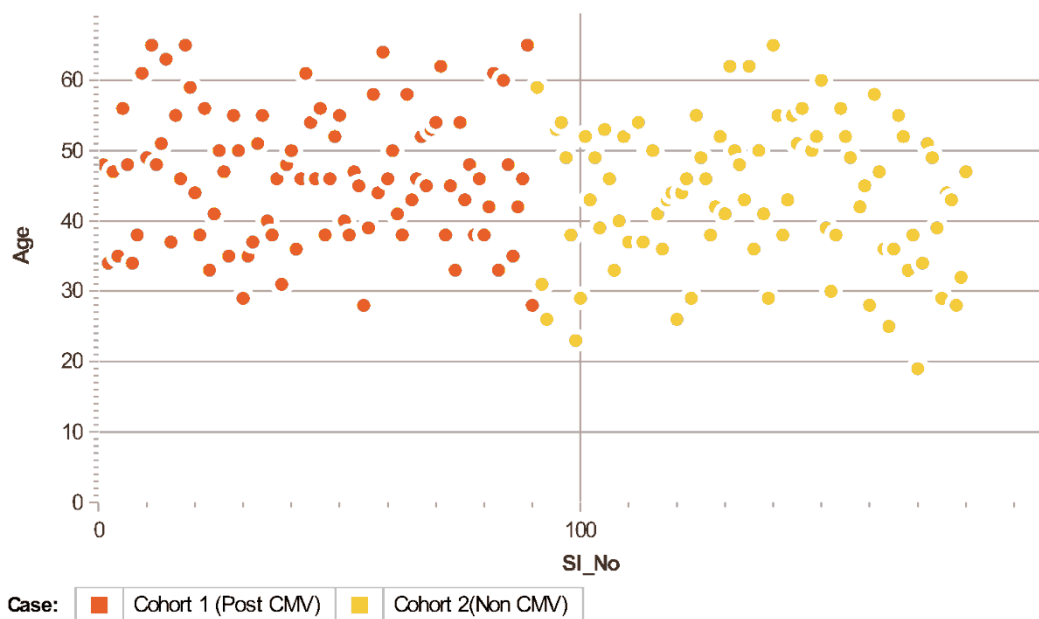
All data were coded and entered in an excel sheet and analyzed using Statistics pack of MS Excel 2016 and statacalc online calculators. Quantitative data analysed with mean, standard deviation and Student T test. Qualitative data analysed with Chi square test.

OBSERVATIONS AND RESULTS

DEMOGRAPHY

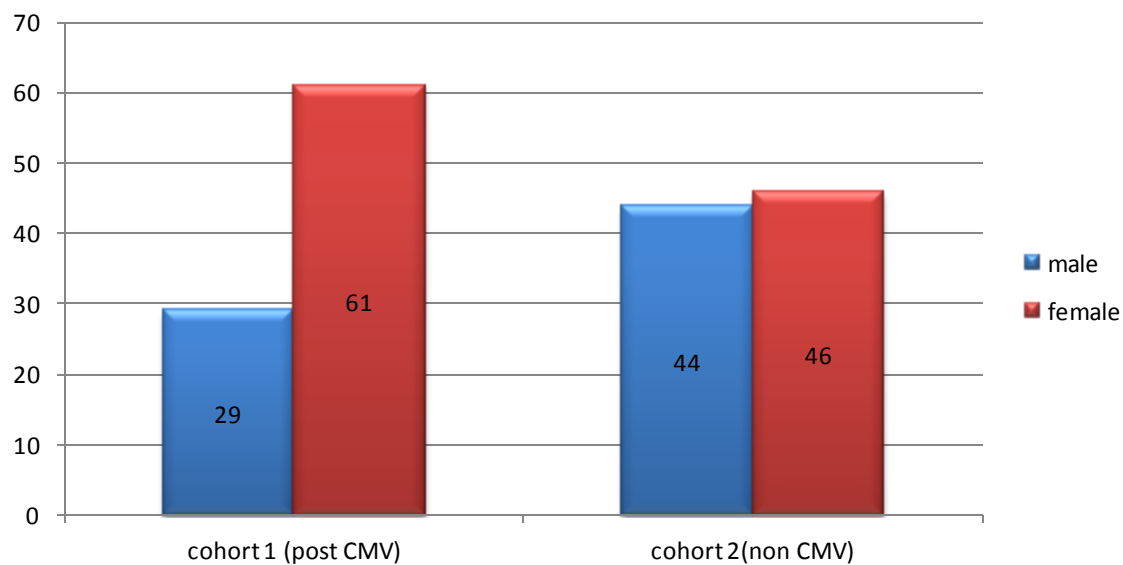
Parameter	Cohort 1 (POST CMV)	Cohort 2 (NON CMV)	Test of significance
Age	46.36 (SE-0.991)	43.87 (SE-1.057)	T test = 1.717 ;p-value = 0.088
Height	155.27 (SE-0.990)	157.08 (SE-0.934)	T test= -1.330 ; p-value = 0.185
Weight	53.933 (SE-1.0414)	54.278 (SE-1.1064)	T test=-0.227 ;p-value = 0.821

Age distribution



Both the cohorts have similar distribution of age, height and weight.

GENDER



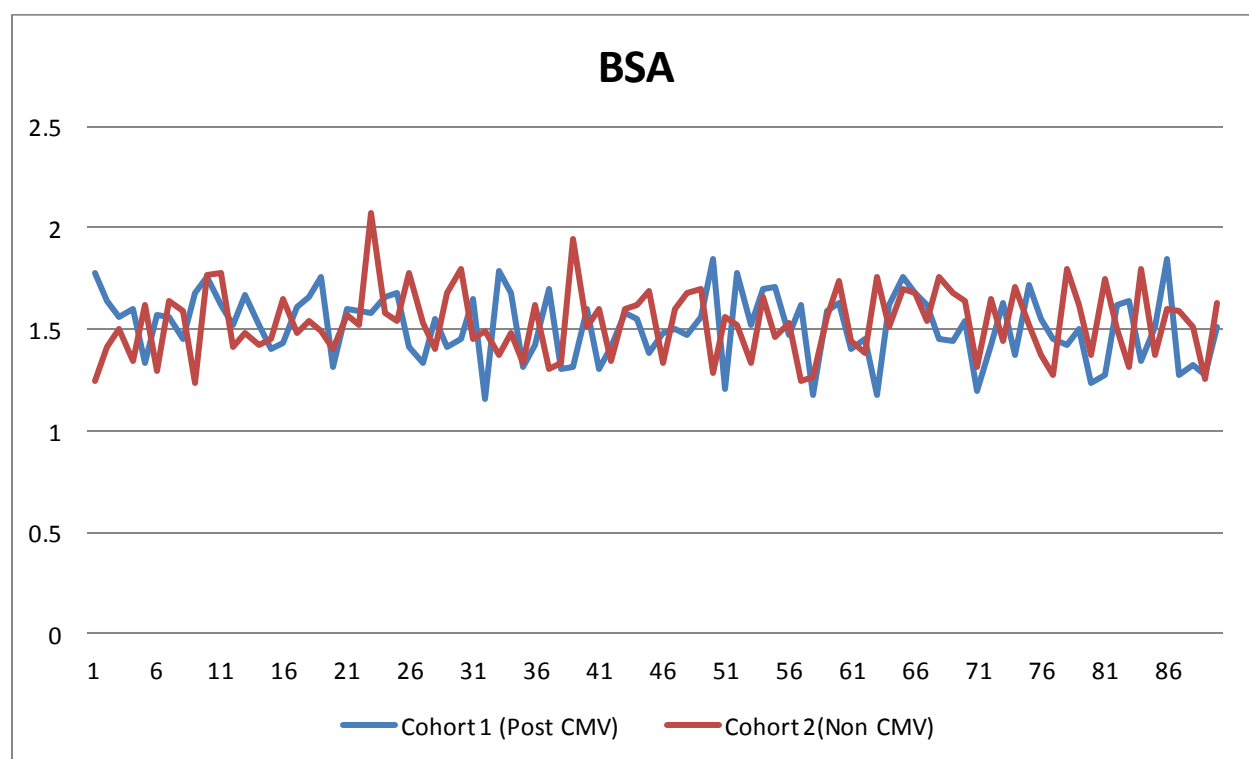
	Cohort 1 (POST CMV)	Cohort 2 (NON CMV)
Male	29	44
Female	61	46
Chi-square test value 5.185 ; p-value = 0.03		

In the CMV cohort (n= 90), the number of females were 61 and in the non CMV cohort (n=90), the number of females were 46. The difference is statistically significant

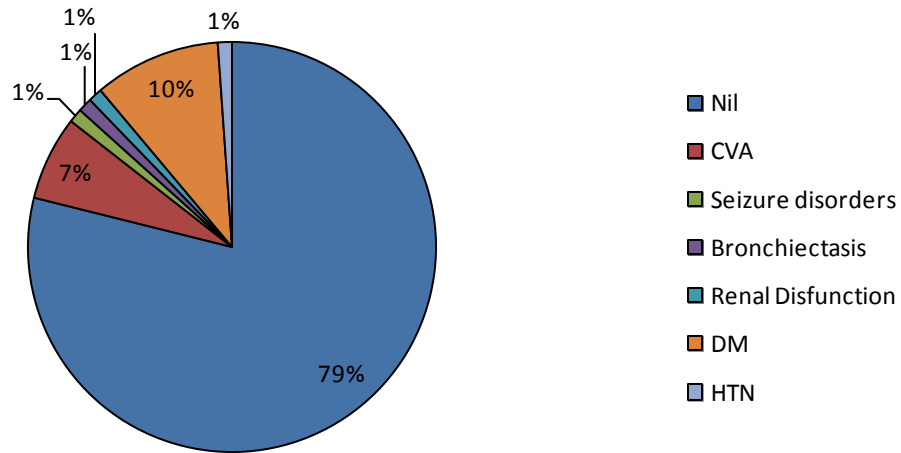
BODY SURFACE AREA

	Cohort 1 (POST CMV)	Cohort 2 (NON CMV)
BSA	Mean = 1.512 (SE- 0.018)	Mean = 1.535 (SE - 0.020)

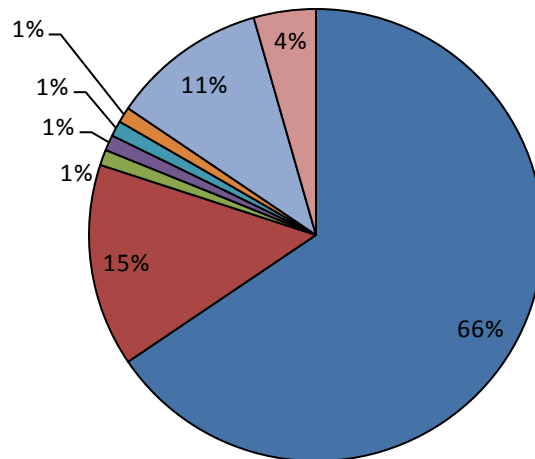
Both the cohorts had patients with similar BSA.



Comorbidities in Cohort 1(Post CMV)



Comorbidities in Cohort 2 (Non CMV)



FUNCTIONAL CLASS OF THE PATIENTS

	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
1	0	1
2	44	48
3	38	40
4	8	1

Most of the patients in both the cohorts belonged to functional class 2 and 3.

PREOPERATIVE RHYTHM

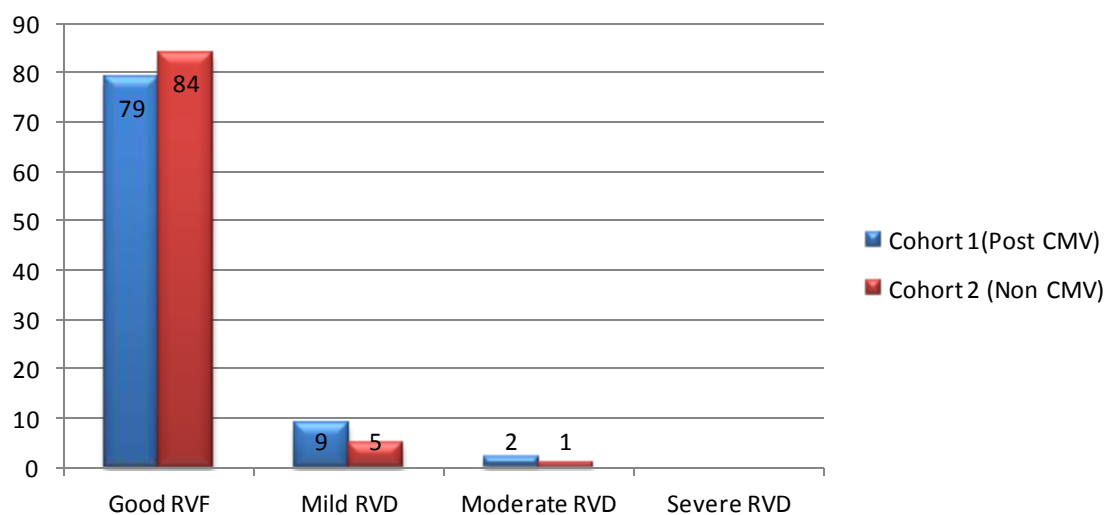
	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
Sinus Rhythm	30	41
AF	59	47
Paroxysmal AF	1	1
CHB	0	1

The prevalence of atrial fibrillation was similar in both the cohorts.

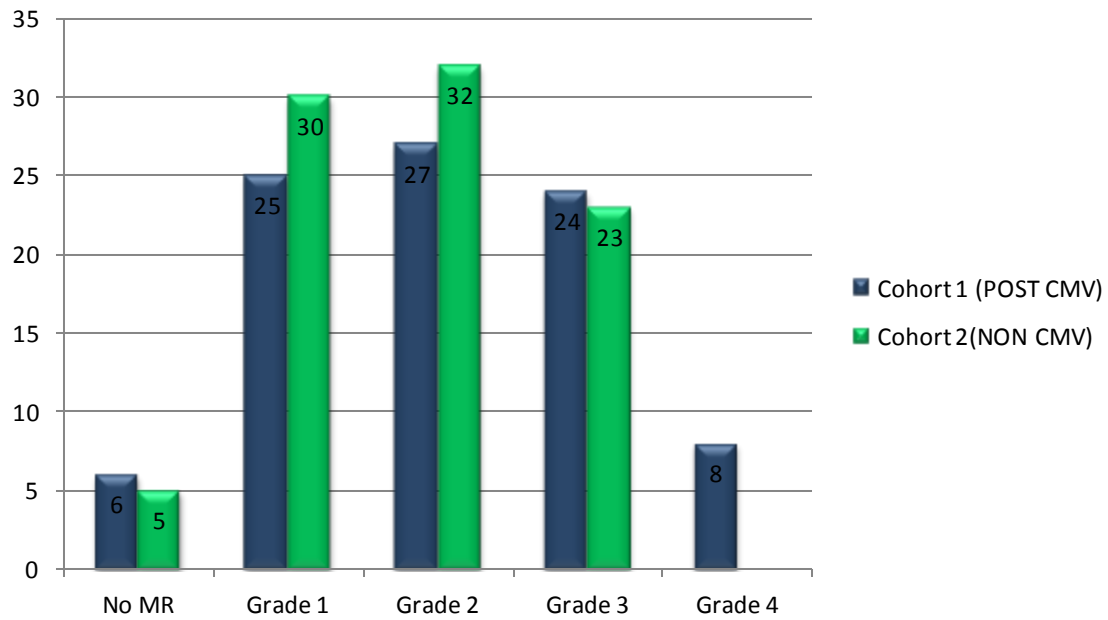
PREOPERATIVE ECHOCARDIOGRAPHIC PARAMETERS

Pre OP Echo Evaluation	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
EF	Mean 62.41 (SE-0.936) (Min 36 – Max 87)	Mean 63.14 (SE-0.874) (Min 37- Max 87)
MS mean	Mean 13.11 (SE-0.510) (Min 4 – Max 30)	Mean 14.76 (SE- 0.609) (Min 3 – Max 30)
LA Size	Mean 53.22 (SE-1.407) (Min 30 – Max 110)	Mean 50.50 (SE- 0.893) (Min 30 – Max 70)
RVSP	Mean 47.93 (SE- 2.138) (Min 0 – Max 110)	Mean 43.62 (SE- 2.812) (Min 0- Max 130)

Right Ventricular Function



Mitral Regurgitation



The preoperative echocardiographic parameters were similar in both the cohorts

INTRAOPERATIVE PARAMETERS

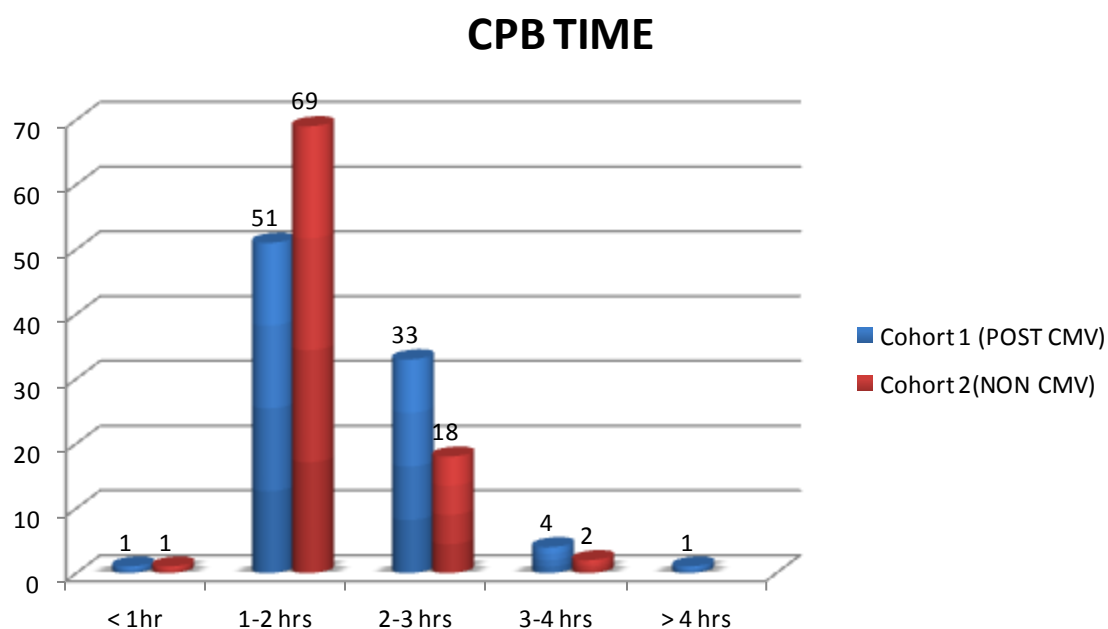
CARDIOPULMONARY BYPASS TIME

CPB Time	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
< 1hr	1	1
1-2 hrs	51	69
2-3 hrs	33	18
3-4 hrs	4	2
> 4 hrs	1	0

	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
CPB TIME	Median - 111.50 (Min 57- Max 269)	Median - 97.00 (Min 57 – Max 227)

According to Mann-Whitney-U test there is significant difference between the groups. (p- value 0.03)

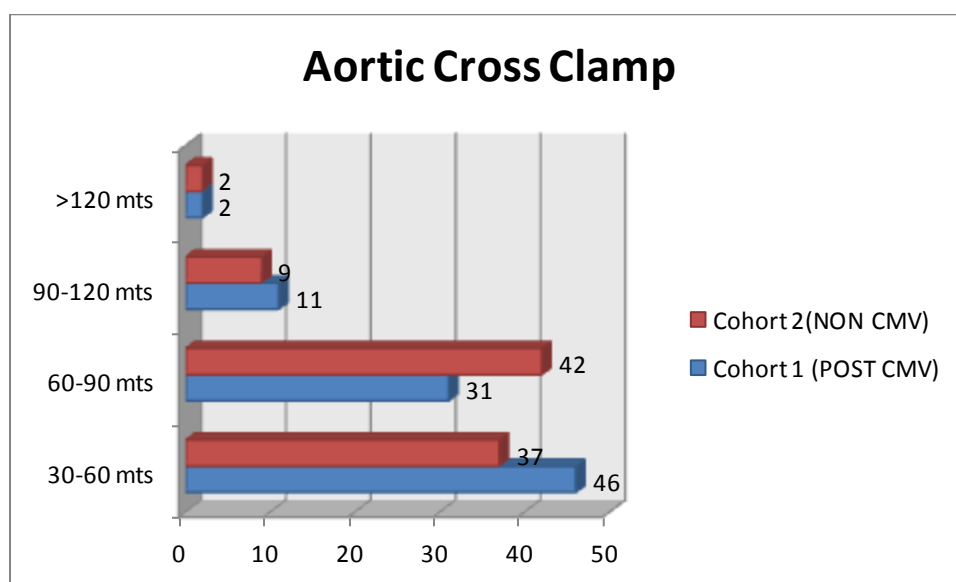
CMV cohort had longer CPB time.



AORTIC CROSS CLAMP TIME

ACC	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
30-60 mts	46	37
60-90 mts	31	42
90-120 mts	11	9
>120 mts	2	2

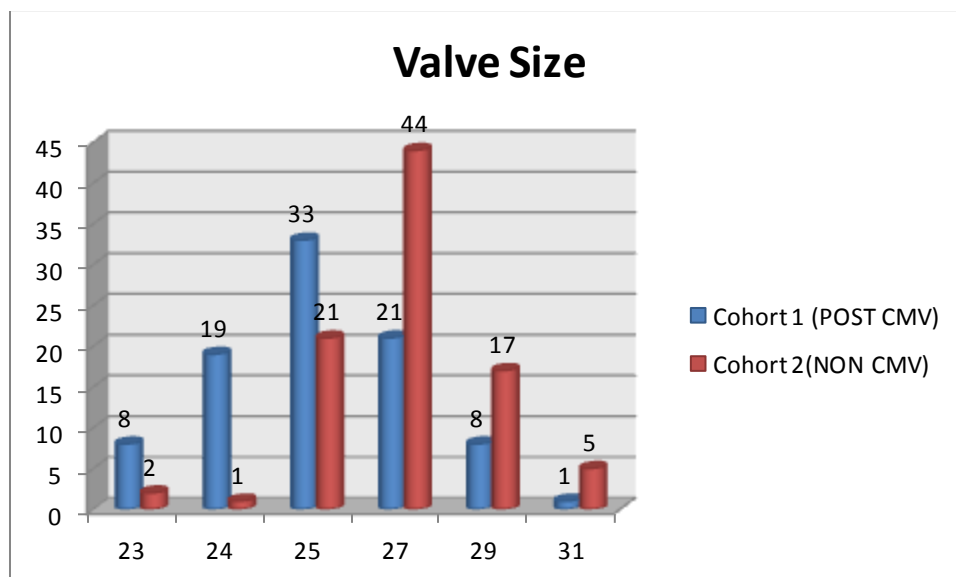
Pearson Chi-Square value 2.833 df (3) p-value = 0.418.* not significant



There is no statistically significant difference in aortic cross clamp time between the two cohorts

VALVE SIZE

Valve Size	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
23	8	2
24	19	1
25	33	21
27	21	44
29	8	17
31	1	5



VALVE TYPE

Valve Type	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
CHVP	22	20
SJM	65	67
PM	1	2
MEDTRONIC	1	1
SEP	1	0

SUBVALVULAR PATHOLOGY

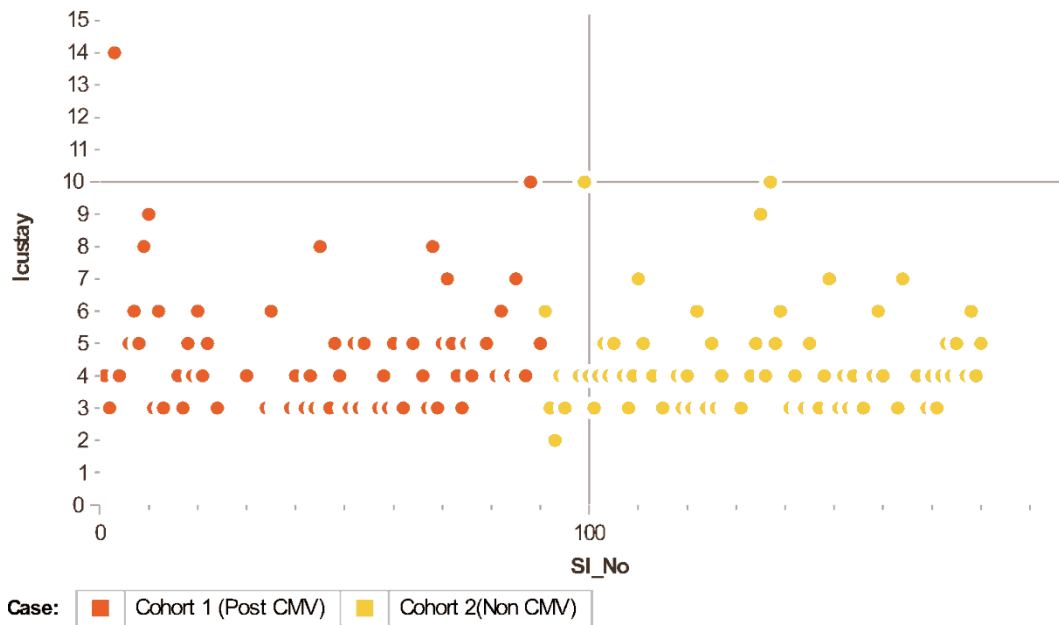
Sub Valvular pathology	Cohort 1 (POST CMV)	Cohort 2(NON CMV)
Present	83	78
Absent	7	12
Chi-square test value = 1.471; p-value = 0.332 .*not significant		

IMMEDIATE POST OPERATIVE PARAMETERS

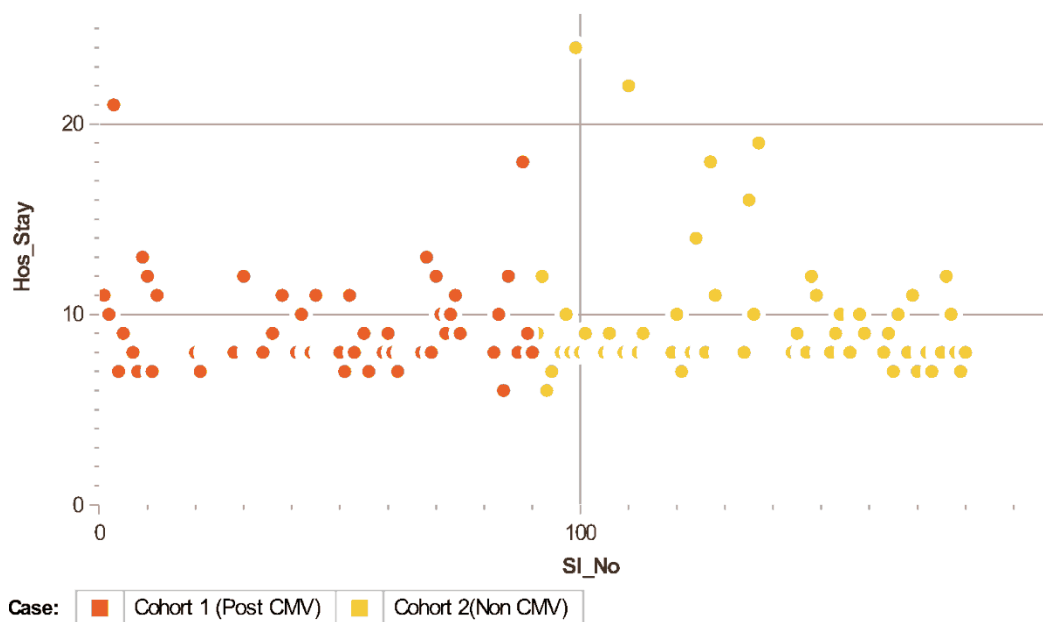
VENTILLATION

Ventilation		
Cohort 1 (POST CMV)	Median - 16.35	Min 3 – Max 120
Cohort 2(NON CMV)	Median - 13.75	Min 4 – Max 56
Mann-Whitney U test ; p-value = 0.154 .*not significant		

DURATION OF ICU STAY



DURATION OF HOSPITAL STAY



The duration of mechanical ventilation, length of ICU stay and duration of hospital stay were similar in both the cohorts.

IONOTROPE REQUIREMENT

Ionotropic Score	Mean	Std. Deviation	Std. Error Mean
Cohort 1 (POST CMV)	11.972	9.3377	.9843
Cohort 2 (NON CMV)	9.572	5.8739	.6192

Independent Samples Test value = 2.064; p-value = 0.040

The post CMV cohort had higher Inotropic requirement.

RIGHT VENTRICULAR FUNCTION IN THE IMMEDIATE POST OPERATIVE PERIOD

	Immediate Post OP RVFunction		Total
	Good RVF	Mild RVD	
Cohort 1 (POST CMV)	84	6	90
Cohort 2(NON CMV)	87	3	90
Total	171	9	180
Pearson Chi-Square = 1.053 p-value=0.305			

RIGHT VENTRICULAR FUNCTION AT ONE YEAR

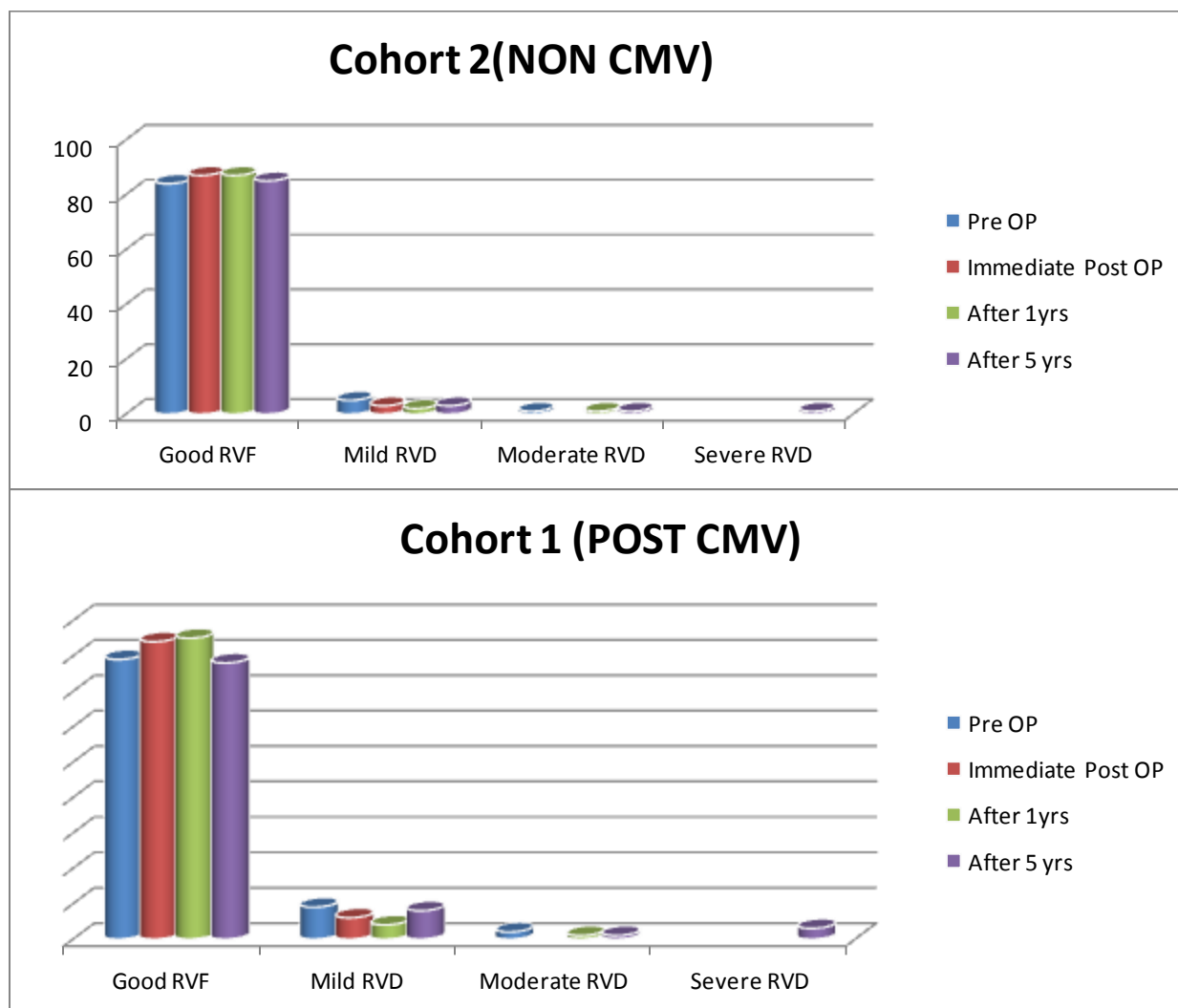
	RVFunction at 1 year				Total
	Good RVF	Mild RVD	Moderate RVD	Severe RVD	
Cohort 1 (POST CMV)	85	4	1	0	90
Cohort 2(NON CMV)	87	2	0	1	90
Total	172	6	1	1	180
Pearson Chi-Square value = 2.690 p-value = 0.442					

RIGHT VENTRICULAR FUNCTION AT 5 YEARS

	RVFunction at 5 years				Total
	Good RVF	Mild RVD	Moderate RVD	Severe RVD	
Cohort 1 (POST CMV)	78	8	1	3	90
Cohort 2(NON CMV)	85	3	1	1	90
Total	163	11	2	4	180
Pearson Chi-Square value = 3.573 p-value = 0.311					

The RV function on follow up at one year and 5years was similar in both cohorts

RIGHT VENTRICULAR FUNCTION



PAH

PAH IN THE IMMEDIATE POSTOPERATIVE PERIOD

	Immediate Post OP PAH		Total
	Nil	Present	
Cohort 1 (POST CMV)	74	16	90
Cohort 2(NON CMV)	82	8	90
Total	156	24	180

Pearson Chi-Square value = 3.077 p-value = 0.079

PAH AT ONE YEAR

	PAH at 1 year		Total
	Nil	Present	
Cohort 1 (POST CMV)	82	8	90
Cohort 2(NON CMV)	86	4	90
Total	168	12	180

Pearson Chi-Square value = 1.429; p-value = 0.232

PAH AT 5 YEAR

	PAH at 5 year		Total
	Present	Absent	
Cohort 1 (POST CMV)	10	80	90
Cohort 2(NON CMV)	6	84	90
Total	16	164	180

Pearson Chi-Square value = 1.098, p-value = 0.295

The PAH on follow up at one year and 5 years was similar in both cohorts.

DISCUSSION

DISCUSSION

A total of 104 patients satisfied the inclusion criteria for the CMV cohort and their records were followed up. Out of the 104, 12 patients were lost to follow up and 2 patients died due to myocardial dysfunction in the immediate post-operative period. 90 patients were studied in the CMV cohort. The same number (n=90) of patients were included in the non CMV cohort.

In the CMV cohort, 67 % were females and in the non CMV cohort 48% were females and this difference is statistically significant. Delaying the valve replacement by performing closed mitral valvotomy is beneficial in female patients in the child bearing age group.

The mean age at which mitral valve replacement was done in the CMV cohort was 46.3 years and in the non CMV cohort was 43.87 years. The disease process started in CMV cohort earlier as most of the patients had CMV at least 10 years prior to presenting for mitral valve replacement.

The mean height and weight were similar in both the cohorts. The two cohorts had a mean body surface area of 1.5 m².

Most of the patients presented with functional class 2 & 3 in both the cohorts, prior to surgery.

65% of the patients in the CMV cohort had preoperative atrial fibrillation, whereas 52% patients in the non CMV cohort presented with atrial fibrillation. This difference was not statistically significant.

Preoperative echocardiographic assessment revealed a mean ejection fraction of 62% & 63%, mean mitral stenosis gradient of 13 mm Hg & 14.7 mm Hg, mean left atrial size of 53.2 mm &

50.5 mm and right ventricular systolic pressure of 47.5 mm Hg & 43.6 mm Hg in post CMV cohort and in the non CMV cohorts respectively.

More than 87% of the patients in both the cohorts had good right ventricular function in the preoperative period.

The CMV cohort had a longer cardiopulmonary bypass time (111.5 minutes) in comparison with the non CMV cohort (97 minutes) and this difference is statistically significant and can be explained by the longer dissection time required for the post closed mitral valvotomy patients.

The aortic cross clamp time remained similar in both the cohorts and this is indicative of the operating time.

36% of the post CMV cohort patients had a valve size of 25 and 48% of patients belonging to non CMV cohort had a valve size of 27 and this difference is not clinically and statistically significant. Sixty five patients in post CMV cohort and 67 patients in the non CMV cohort received St Jude prosthetic valve. Twenty two patients in post CMV cohort and twenty patients from the non CMV cohort received Chitra heart valve prosthesis.

The percentage of subvalvar pathology was 88 in both the cohorts.

Patients belonging to post CMV cohort had a median ventilation time of 16.35 hours and the patients of the non CMV cohort had a median ventilation time of 13.75 hours and the difference is not statistically significant. The duration of ICU stay and length of hospital stay are comparable in both the cohorts.

Inotropic requirement, measured by the vasoactive inotropic score, was higher in the post CMV group (11.9) when compared to the other cohort (9.7) and this difference is statistically significant.

Right ventricular function and pulmonary arterial hypertension assessed in the immediate postoperative period, at one year and at five years does not show any significant difference.

CONCLUSION

CONCLUSION

The percentage of females in the CMV cohort is higher and this difference is statistically significant. Delaying the valve replacement by performing a surgical palliative procedure like closed mitral valvotomy, is beneficial in female patients in the child bearing age group.

The percentage of atrial fibrillation and preoperative echocardiographic parameters were similar in both the cohorts. Therefore, CMV prevented progression of the disease in CMV group.

The CMV cohort had a longer cardiopulmonary bypass time which is statistically significant and is due to the longer dissection time required for the post closed mitral valvotomy patients. However the aortic cross clamp time is similar in both the cohorts.

The duration of ICU stay and hospital stay was similar in both cohorts.

The inotropic requirement was higher in the post CMV group and it is statistically significant.

Right ventricular function and pulmonary arterial hypertension assessed in the immediate postoperative period, at one year and at five years showed the same progression in both cohorts.

LIMITATIONS

As it was retrospective study some patients were lost to follow up.

Some of the patients could not be studied because of incomplete data.

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श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)

Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

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

SCT/IEC/1226/JUNE-2018

24.07.2018

Dr. Renjith S
Senior Resident
Department of CVTS
SCTIMST, Thiruvananthapuram

Dear Dr. Renjith,

The Institutional Ethics Committee reviewed your application to conduct the study entitled "OUTCOMES OF POST CLOSED MITRAL VALVOTOMY MITRAL VALVE REPLACEMENT- A RETROSPECTIVE COHORT STUDY (IEC/1226)" on 24th July, 2018.

Original submission

1. Covering letter addressed to the Chairman, IEC, SCTIMST with check list
2. TAC Approval Letter dated 29.05.2018
3. IEC Application Form
4. Project Proposal
5. CV of Principal Investigator and Co-Principal Investigators

Revised submission

1. Covering letter addressed to the Chairman, IEC, SCTIMST dated 02.07.2018 with checklist
2. Forwarding Letter from the HOD dated 13.07.2018
3. TAC Approval Letter dated 25.06.2018
4. IEC Application Form
5. Project Proposal
6. Proforma
7. CV of Principal Investigator and Co-Principal Investigators

The IEC Review Criteria

The study was reviewed using an expedited procedure with the permission of the Chairman to allow for submission requirement for DM/MCh final year residents wherein students were required to submit dissertation before July 31, 2018.

IEC Decision

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

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,

Mala Ramanathan
Member Secretary, IEC

PROFORMA

UNIQUE ID

1. AGE

2. SEX

3. HEIGHT

4. WEIGHT

5. BSA

6. COMORBIDITIES

- a) DIABETES MELLITUS (DM)
- b) HYPERTENSION (HTN)
- c) OTHERS

8. DURATION OF DISEASE

9. TIME PERIOD BETWEEN ONSET OF DISEASE AND CMV

10. TIME PERIOD BETWEEN CMV AND MVR

PREOPERATIVE DETAILS

11. FUNCTIONAL CLASS

12. PREOPERATIVE RHYTHM

13. PREOPERATIVE ECHOCARDIOGRAPHY

- a) EJECTION FRACTION (EF)
- b) MITRAL STENOSIS GRADIENT
- c) MR
- d) LA
- e) AORTA
- f) TR
- g) RVSP
- h) RV FUNCTION

INTRAOPERATIVE DETAILS

14. CARDIOPULMONARY BYPASS TIME

15. AORTIC CROSS CLAMP TIME

16. VALVE SIZE

17. SUBVALVULAR PATHOLOGY

POSTOPERATIVE DETAILS

18. HOURS OF VENTILLATION

19. DAYS IN ICU

20. NUMBER OF DAYS OF HOSPITAL STAY

21. IONOTROPIC SCORE

22. RHYTHM

23. POST OPERATIVE ECHOCARDIOGRAPHY

IMMEDIATE

1 YEAR

5 YEAR

- a) MS GRADIENT
- b) MR
- c) EF
- d) RVFUNCTION (TAPSE)
- e) TR
- f) PAH
- g) LA
- h) AORTA

Sl No	unique id	case	AGE	SEX	HEIGHT	WEIGHT	BSA	DM	HTN	OTHERS	FN CLASS	RHYTHM	EF	MS PEAK	MS MEAN	MR	LA	AORTA	TR	RVSP	RV FUN	CPB TIME	ACC	VALVE SIZE	VALVE	SUB VAL	VENTIL	ICUSTAY	HOS STAY	IONOS CORE	RHYTHM	MS GR PEAK 1	MS GR MEAN 1	MR 1	EF1	RVF 1	TR 1	RVSP 1	LA1	AORTA1	MS GR PK 4	MS GR MEAN 4	MR 4	EF4	RVF 4	
1	9377	Cohort 1 (Post CMV)	48	2	148	43	1.32	2	2	3	2	1	68	19	10	2	36	24	2	70	1	100	60	29	1	1	8	4	11	3	1	9	5	1	65	1	1	0	34	28	6	2	3	69	1	
2	8606495	Cohort 1 (Post CMV)	34	1	172	65	1.76	2	2	2	2	1	61	31	10	3	65	27	2	35	1	93	56	29	1	1	6	3	10	0	2	10	4	0	40	1	1	0	42	32	17	6	0	38	1	
3	28810	Cohort 1 (Post CMV)	47	1	171	67	1.78	2	2	2	4	2	48	23	11	3	110	23	1	54	1	161	76	27	2	1	120	14	21	50.5	2	10	4	1	65	1	2	36	78	30	13	3	2	61	1	
4	289920	Cohort 1 (Post CMV)	35	1	155	44	1.37	2	2	2	2	2	57	21	12	1	53	29	1	44	1	125	53	29	2	1	16	4	7	10	2	13	4	2	47	1	1	0	37	27	9	2	1	54	1	
5	22623	Cohort 1 (Post CMV)	56	2	140	46	1.33	1	2	2	3	2	55	16	7	2	50	24	3	57	1	152	96	27	1	1	17	5	9	15	2	17	6	1	58	1	3	53	51	33	12	7	1	62	1	
6	269385	Cohort 1 (Post CMV)	48	1	164	59	1.64	2	2	2	2	2	52	10	6	1	54	42	2	40	1	106	55	29	2	2	18	5	8	15	2	10	4	1	54	1	1	35	51	39	16	7	1	52	1	
7	276139	Cohort 1 (Post CMV)	34	1	167	60	1.66	2	2	3	1	1	55	35	20	3	53	21	2	62	1	145	82	27	2	1	25	6	8	35	1	5	2	1	76	1	1	0	40	28	11	4	1	67	1	
8	280495	Cohort 1 (Post CMV)	38	2	150	41	1.31	2	2	2	3	2	52	22	9	3	48	24	4	35	2	164	57	23	2	1	27	5	7	26	2	17	5	0	62	2	2	22	48	28	20	7	1	70	1	
9	278597	Cohort 1 (Post CMV)	61	2	155	53	1.51	2	2	2	2	2	68	29	13	3	55	27	1	40	1	184	82	31	1	1	14	8	13	20	2	6	4	1	58	1	2	53	44	31	3	1	2	73	1	
10	30906	Cohort 1 (Post CMV)	49	2	149	51	1.45	2	2	3	3	3	66	27	16	3	60	24	1	48	1	144	101	29	1	1	8	9	12	10	1	11	6	0	69	1	2	30	38	21	11	4	1	68	1	
11	296137	Cohort 1 (Post CMV)	65	2	149	60	1.57	1	2	2	2	1	76	23	16	2	50	30	1	45	1	185	136	25	3	2	16	3	7	5	1	11	4	0	65	1	1	40	35	26	7	4	1	62	1	
12	8605990	Cohort 1 (Post CMV)	48	2	154	62	1.68	1	2	2	3	2	56	32	19	3	52	28	0	0	1	269	112	29	1	1	20	6	11	20	2	7	4	0	70	1	0	0	44	32	13	4	1	77	1	
13	8606055	Cohort 1 (Post CMV)	51	2	148	53	1.47	2	2	2	3	3	73	36	18	3	47	23	1	20	1	84	46	27	2	1	18	3	8	20	1	13	4	1	70	1	1	34	42	25	14	5	1	63	1	
14	286915	Cohort 1 (Post CMV)	63	1	157	59	1.62	2	2	2	3	2	54	16	10	1	41	32	2	51	3	96	58	27	2	1	25	4	8	20	2	8	4	1	61	1	0	0	48	28	11	7	1	40	1	
15	9106234	Cohort 1 (Post CMV)	37	1	165	58	1.63	2	2	2	3	2	74	28	15	2	51	27	2	57	1	141	91	29	2	1	18	4	8	15	2	9	3	0	61	1	0	0	48	32	12	6	1	80	1	
16	223635	Cohort 1 (Post CMV)	55	2	147	62	1.59	2	2	2	2	3	70	20	11	1	52	28	1	45	1	112	63	31	2	1	17	4	8	5	1	7	3	1	65	1	1	0	43	25	5	2	1	70	1	
17	16346	Cohort 1 (Post CMV)	46	2	149	66	1.62	2	2	2	2	1	59	24	12	2	50	30	2	40	1	121	72	27	1	1	16	3	8	5	1	15	5	2	65	1	2	32	47	24	9	4	1	54	1	
18	9102208	Cohort 1 (Post CMV)	65	2	141	41	1.3	2	2	2	2	3	65	20	14	1	51	29	1	86	2	126	62	25	2	1	18	5	8	40	2	7	3	0	70	1	2	46	45	25	7	3	1	71	1	
19	285575	Cohort 1 (Post CMV)	59	1	168	60	1.7	2	2	2	3	2	46	23	14	3	53	23	3	53	1	101	61	27	2	1	18	4	8	15	2	11	5	1	59	1	1	32	46	28	9	4	0	67	1	
20	279223	Cohort 1 (Post CMV)	44	1	163	58	1.62	1	2	3	2	2	60	28	13	3	101	34	3	45	1	120	69	27	2	1	11	6	8	10	2	8	3	0	48	1	2	30	65	28	7	3	1	55	1	
21	295482	Cohort 1 (Post CMV)	38	2	149	41	1.3	2	2	2	2	2	62	36	21	1	48	27	3	68	1	132	66	27	2	1	17	4	7	10	2	19	6	2	58	1	2	26	41	21	20	7	1	63	1	
22	32202	Cohort 1 (Post CMV)	56	2	155	51	1.48	1	2	2	2	1	63	34	19	2	55	24	3	79	1	95	46	29	2	1	21	5	8	40	1	10	7	0	62	1	0	0	50	23	15	10	2	41	1	
23	304653	Cohort 1 (Post CMV)	33	1	164	70	1.78	2	2	2	2	1	63	14	7	0	41	21	0	33	1	86	50	27	2	1	19	3	8	20	1	8	4	1	69	1	0	0	43	31	13	5	1	60	1	
24	281278	Cohort 1 (Post CMV)	41	1	169	62	1.7	2	2	2	3	2	60	21	12	0	54	29	2	34	1	85	51	29	2	1	12	3	8	13	2	14	5	1	58	1	3	25	34	32	11	2	0	64	1	
25	263658	Cohort 1 (Post CMV)	50	2	148	49	1.41	2	2	2	3	1	61	28	18	2	46	22	4	110	1	88	56	27	2	1	22.5	4	8	20	1	8	7	1	73	1	1	0	35	22	9	4	1	74	1	
26	243137	Cohort 1 (Post CMV)	47	2	155	57	1.56	2	2	3	2	2	70	26	12	3	59	24	3	34	1	62	38	25	2	1	17	4	8	12	2	12	4	1	68	1	2	25	43	27	13	4	0	55	1	
27	308531	Cohort 1 (Post CMV)	35	2	158	55	1.55	2	2	2	3	1	62	18	11	2	46	24	2	77	1	87	56	27	1	1	12	4	8	10	1	7	3	1	63	1	1	38	34	26	8	5	0	75	1	
28	291645	Cohort 1 (Post CMV)	55	1	169	45	1.45	2	2	2	3	2	60	28	11	4	64	25	2	29	1	110	60	27	1	1	18	4	8	15	2	10	4	1	61	1	2	20	62	30	10	4	1	62	1	
29	267917	Cohort 1 (Post CMV)	50	2	145	65	1.61	2	2	7	3	2	68	29	11	3	58	26	4	32	2	88	53	25	5	1	12	4	12	10	2	12	4	1	57	2	4	45	54	27	15	7	0	56	1	
30	300885	Cohort 1 (Post CMV)	29	2	156	56	1.56	2	2	2	2	2	58	28	11	3	47	28	3	55	1	141	75	27	2	1	19	4	12	25	2	7	4	2	60	1	2	30	41	26	17	7	1	73	1	
31	8907082	Cohort 1 (Post CMV)	35	2	152	46	1.4	2	2	2	2	2	45	17	8	4	69	24	4	37	1	120	61	31	2	1	12	3	8	10	2	12	4	2	61	2	3	30	64	28	12	5	1	40	2	
32	259706	Cohort 1 (Post CMV)	37	2	160	66	1.71	2	2	2	2	1	80	47	24	2	52	27	2	38	1	152	72	25	1	1	22	3	8	1	1	9	4	1	61	1	2	40	46	29	13	8	1	55	1	
33	268489	Cohort 1 (Post CMV)	51	1	156	55	1.54	2	2	2	4	2	61	21	6	3	49	23	4	22	1	169	90	25	2	2	10.5	3	8	20	2	12	3	1	52	1	2	22	49	23	12	4	1	55	1	
34	286169	Cohort 1 (Post CMV)	55	2	148	34	1.18	2	2	2	2	2	69	35	19	2	44	33	2	50	1	168	59	27	2	1	15.5	3	8	2	2	6	3	1	60	1	1	0	46	34	9	3	0	60	1	
35	38468	Cohort 1 (Post CMV)	40	1	158	55	1.55	2	2	2	2	1	75	28	17	2	41	24	2	44	1	79	45	27	2	1	9	6	9	2	1	11	4	1	58	1	1	38	32	27	11	5	0	66	1	
36	263058	Cohort 1 (Post CMV)	38	2	152	57	1.55	2	2	2	3	2	54	31	19	2	47	24	2	35	1	119	62	27	1	1	13	3	9	10	2	10	5	1	43	1	1	20	43	25	18	5	1	53	1	
37	314158	Cohort 1 (Post CMV)	46	2	161	59	1.62	1	2	2	4	1	55	32	19	1	40	31	1	54	1	87	56	25	2	1	12.5	3	11	5	2	12	6	1	50	1	3	36	40	28	22	6	11	0	70	1
38	310002	Cohort 1 (Post CMV)	31	2	165	46	1.45	2	2	2	3	2	58	14	9	4	69	25	4	33</																										

66	9302255	Cohort 1 (Post CMV)	46	1	168	67	1.76	2	2	2	2	2	59	2	12	1	60	28	3	42	1	64	40	25	2	2	6	4	8	7	2	18	10	1	50	1	1	36	60	27	18	10	1	50	2	
67	311071	Cohort 1 (Post CMV)	52	2	156	68	1.58	2	2	2	2	2	58	28	10	2	49	28	1	20	1	115	59	27	2	1	11	3	8	5	2	20	8	1	69	1	2	32	50	26	18	6	1	60	1	
68	33029	Cohort 1 (Post CMV)	45	1	167	68	1.76	1	2	2	2	2	66	27	12	2	55	25	2	40	1	181	81	27	2	1	43	8	13	25	2	9	4	0	64	1	1	20	50	25	11	4	0	66	1	
69	8701470	Cohort 1 (Post CMV)	53	2	155	38	1.31	2	2	2	3	2	64	26	11	2	49	21	1	40	1	83	67	25	2	1	12	3	8	5	2	12	5	1	62	1	1	0	44	27	12	6	1	63	1	
70	259291	Cohort 1 (Post CMV)	54	2	133	66	1.68	2	2	2	3	1	60	17	9	1	49	28	1	16	1	157	64	25	2	2	16	5	12	10	1	1	8	4	1	55	1	1	18	43	27	11	4	0	67	1
71	270106	Cohort 1 (Post CMV)	62	2	148	62	1.23	2	2	2	2	2	54	12	5	1	63	24	4	42	1	138	80	25	2	2	46	7	10	10	2	17	7	2	80	1	2	28	52	23	18	7	0	60	1	
72	8805188	Cohort 1 (Post CMV)	38	1	162	56	1.58	2	2	2	2	2	60	21	14	3	55	25	1	48	1	133	83	31	1	1	17	5	9	5	2	5	3	1	59	1	2	24	54	24	12	4	1	60	1	
73	239372	Cohort 1 (Post CMV)	45	2	152	33	1.18	2	2	2	3	1	55	18	11	1	101	80	2	50	2	165	110	31	1	1	18	4	10	10	1	9	4	2	58	1	2	42	46	32	9	3	2	80	1	
74	267607	Cohort 1 (Post CMV)	33	2	160	63	1.67	2	2	2	2	1	62	21	13	3	52	20	2	78	1	110	58	29	1	1	7	3	11	10	1	9	3	2	65	1	2	36	38	28	8	3	2	70	1	
75	9201891	Cohort 1 (Post CMV)	54	2	147	53	1.47	2	2	2	2	2	52	22	11	1	68	30	4	28	1	155	80	32	6	1	22	5	9	20	2	10	4	0	70	1	2	30	58	26	12	4	0	57	1	
76	271508	Cohort 1 (Post CMV)	43	2	149	36	1.2	2	2	2	3	2	56	18	10	0	46	19	2	41	1	88	39	29	2	1	17	4	8	10	2	8	3	2	77	1	2	40	42	30	13	6	0	53	1	
77	8605098	Cohort 1 (Post CMV)	48	2	133	54	1.51	2	2	2	2	1	66	38	18	2	42	24	1	20	1	104	51	27	1	1	17	5	8	10	1	10	3	0	80	1	1	0	40	23	19	10	0	58	1	
78	9009057	Cohort 1 (Post CMV)	38	2	157	63	1.6	2	2	2	3	1	58	23	4	2	42	26	2	60	1	148	98	29	1	1	14	5	8	20	1	9	6	1	74	1	0	0	43	24	8	3	1	69	1	
79	265656	Cohort 1 (Post CMV)	46	2	149	50	1.45	2	2	2	3	1	60	33	19	4	40	20	3	100	2	93	54	25	2	1	18	5	8	10	1	4	2	0	58	1	2	26	39	26	12	5	0	66	1	
80	8702326	Cohort 1 (Post CMV)	38	2	150	49	1.42	2	2	2	3	1	56	16	8	2	47	24	2	42	1	106	51	27	2	1	17	4	8	10	1	10	4	1	56	2	2	31	42	23	9	4	0	71	1	
81	269818	Cohort 1 (Post CMV)	42	2	156	61	1.62	2	2	5	3	2	64	25	10	4	54	30	2	50	1	83	56	29	2	1	13	4	8	7	2	12	4	1	73	1	2	20	51	27	16	6	0	69	1	
82	8808816	Cohort 1 (Post CMV)	61	2	144	58	1.52	2	2	3	2	2	70	25	12	3	62	26	3	44	1	118	57	31	2	1	27	6	8	35	2	17	6	1	55	1	1	38	52	23	20	7	0	51	2	
83	8606920	Cohort 1 (Post CMV)	33	2	154	38	1.27	2	2	2	3	2	45	24	13	1	50	26	2	35	1	144	87	27	1	2	6	4	10	2	2	10	4	2	74	1	0	0	45	25	9	5	0	65	1	
84	8805217	Cohort 1 (Post CMV)	60	2	146	44	1.33	2	2	2	3	2	61	22	11	4	78	27	3	40	1	112	64	31	2	1	18	4	6	5	2	4	2	0	68	1	3	31	54	31	7	3	2	80	1	
85	260092	Cohort 1 (Post CMV)	48	2	145	56	1.63	2	2	2	3	2	60	12	7	0	55	25	4	54	1	230	123	31	2	1	60	7	12	20	2	13	4	0	61	1	2	18	42	25	9	6	1	50	3	
86	249703	Cohort 1 (Post CMV)	35	2	165	62	1.68	2	2	2	2	2	36	20	11	3	62	28	2	45	1	111	70	29	1	1	17	4	8	20	2	6	3	1	54	1	0	0	51	30	12	3	1	67	1	
87	9605687	Cohort 1 (Post CMV)	42	2	161	45	1.42	2	2	2	3	2	62	30	20	3	56	28	3	70	1	128	66	29	1	1	17	4	8	16	2	7	3	1	60	1	0	0	42	27	6	3	1	68	1	
88	283439	Cohort 1 (Post CMV)	46	2	148	36	1.21	2	2	2	3	2	48	20	10	1	57	26	2	64	1	141	94	29	1	1	15.5	10	18	20	2	10	5	0	63	2	3	75	41	22	9	4	1	62	1	
89	9408646	Cohort 1 (Post CMV)	65	2	152	38	1.27	2	2	2	3	2	58	36	23	1	37	22	2	73	1	164	99	27	2	1	16	5	9	12.5	2	4	2	0	54	1	0	0	44	27	7	3	0	65	1	
90	283771	Cohort 1 (Post CMV)	59	1	163	44	1.41	2	2	2	2	1	50	45	30	1	39	24	2	65	1	88	49	27	2	1	17	5	8	10	1	10	4	1	55	1	2	22	40	22	10	4	1	68	1	
91	263188	Cohort 2 (Non CMV)	28	1	143	37	1.24	2	2	2	2	2	50	20	13	2	51	30	3	66	1	135	95	25	1	2	13	6	9	20	2	9	5	0	43	1	3	46	51	34	10	6	2	64	1	
92	278221	Cohort 2 (Non CMV)	31	1	168	43	1.41	2	2	2	3	1	64	34	17	3	68	25	0	0	1	105	70	29	1	1	6	3	12	7	1	8	5	1	67	1	0	0	37	25	13	3	2	80	1	
93	262247	Cohort 2 (Non CMV)	26	1	169	44	1.5	2	2	2	3	1	65	54	30	2	44	33	2	62	1	109	76	27	1	1	5	2	6	5	1	9	4	1	77	1	1	17	36	22	19	9	2	68	1	
94	285345	Cohort 2 (Non CMV)	53	2	139	47	1.34	2	2	3	2	2	50	24	16	3	46	25	3	78	1	98	69	25	2	1	18	4	7	0	2	11	3	1	50	1	2	38	36	22	18	6	1	70	1	
95	256838	Cohort 2 (Non CMV)	53	1	166	57	1.62	2	2	3	3	2	54	18	9	2	44	24	1	27	1	153	103	27	2	1	16	3	8	20	2	9	4	0	61	1	0	0	41	31	11	4	1	62	1	
96	276652	Cohort 2 (Non CMV)	54	2	143	42	1.29	1	2	1	3	2	70	16	10	3	58	27	0	36	1	107	74	27	2	2	17	4	8	3	2	5	3	1	53	1	2	16	42	21	10	5	0	80	1	
97	273525	Cohort 2 (Non CMV)	49	1	160	61	1.64	1	2	3	3	1	62	13	7	3	50	25	0	37	1	104	61	27	5	1	9	4	10	10	1	10	5	1	40	1	0	0	46	27	8	4	0	58	1	
98	280532	Cohort 2 (Non CMV)	38	1	167	55	1.59	2	2	3	2	2	64	23	13	2	56	28	2	23	1	152	102	27	1	1	24	4	8	3	2	7	3	1	49	1	1	20	45	32	9	3	2	45	1	
99	283741	Cohort 2 (Non CMV)	23	2	156	35	1.23	2	2	3	2	2	4	57	20	12	2	54	23	3	73	1	93	63	27	3	1	18	10	24	0	4	13	6	0	77	1	2	20	32	25	14	7	0	77	1
100	217807	Cohort 2 (Non CMV)	29	2	155	73	1.77	2	2	2	2	1	84	15	10	2	41	23	0	0	1	95	53	27	2	1	9	4	8	5	1	8	4	1	54	1	0	0	44	31	10	5	2	72	1	
101	276947	Cohort 2 (Non CMV)	52	1	161	71	1.78	1	2	2	2	2	60	36	19	3	58	38	1	60	1	120	73	27	2	1	10	3	9	10	2	12	5	0	60	1	0	0	55	32	17	5	1	76	1	
102	271761	Cohort 2 (Non CMV)	43	1	161	45	1.41	2	2	2	3	2	62	19	13	3	60	22	1	0	1	148	75	27	2	1	16	4	8	20	2	14	5	0	42	1	1	15	49	24	8	3	0	70	1	
103	275495	Cohort 2 (Non CMV)	49	2	146	54	1.48	2	2	2	3	2	60	40	25	3	47	28	2	57	1	112	61	27	2	1	18	5	8	20	2	7	2	2	75	2	2	21	47	22	12	4	1	82	2	
104	292378	Cohort 2 (Non CMV)	39	1	156	47	1.42	2	2	2	3	1	69	23	15	1	48	26	1	0	1	83	56	27	2	1	18.5	4	8	10																

133	290113	Cohort 2(Non CMV)	48	1	162	57	1.6	2	2	3	2	2	55	15	10	2	61	34	2	33	1	62	39	31	2	1	9	4	8	5	2	7	2	1	45	1	1	16	47	26	19	5	0	55	1
134	315256	Cohort 2(Non CMV)	43	1	158	60	1.62	2	2	2	2	1	65	21	13	1	37	31	0	0	1	108	63	25	2	1	7	5	8	5	1	11	5	1	70	1	0	0	44	32	21	8	0	64	1
135	269940	Cohort 2(Non CMV)	62	1	154	67	1.69	2	1	7	2	2	67	17	11	2	43	29	1	25	1	102	82	29	2	1	20	9	16	5	2	11	5	0	52	1	2	22	52	25	11	4	1	47	1
136	239663	Cohort 2(Non CMV)	36	1	140	46	1.33	2	2	2	2	1	87	16	7	2	30	25	2	40	1	57	40	25	1	1	9	4	10	4	1	5	2	0	64	1	1	20	35	25	12	6	1	69	1
137	209618	Cohort 2(Non CMV)	50	1	171	54	1.6	2	2	3	2	2	37	15	8	1	53	30	3	102	2	227	131	27	1	1	32	10	19	25	2	12	5	0	67	1	2	38	44	24	11	4	1	66	1
138	328970	Cohort 2(Non CMV)	41	1	170	60	1.68	2	2	3	2	1	60	32	22	2	51	23	2	38	1	114	86	27	2	1	7	5	8	0	1	8	3	1	58	1	0	0	40	30	9	3	1	62	1
139	322817	Cohort 2(Non CMV)	29	1	161	65	1.7	2	2	2	2	1	73	35	19	1	48	25	2	70	1	93	63	27	2	1	12	6	8	5	1	11	4	1	64	1	3	36	42	24	14	7	1	76	1
140	246941	Cohort 2(Non CMV)	65	2	148	40	1.28	1	2	2	2	2	72	29	13	2	55	35	2	50	1	67	50	25	3	1	9	3	8	7	2	12	4	0	64	1	1	34	51	34	11	5	0	74	1
141	327051	Cohort 2(Non CMV)	55	2	150	59	1.56	2	2	3	2	1	66	35	26	1	48	24	2	78	1	74	55	27	2	1	8	3	8	5	1	9	4	1	62	1	1	35	47	31	10	3	1	67	1
142	323408	Cohort 2(Non CMV)	38	2	161	52	1.52	2	2	2	2	1	54	22	18	0	45	24	0	0	1	112	76	25	2	1	5	4	8	5	1	11	6	1	80	1	0	0	38	25	9	4	0	60	1
143	295820	Cohort 2(Non CMV)	43	2	153	42	1.33	2	2	3	2	2	65	33	20	2	45	29	3	98	1	72	43	27	2	1	7	3	8	0	2	11	6	0	64	1	3	63	46	26	13	5	1	57	1
144	334955	Cohort 2(Non CMV)	55	2	154	65	1.66	1	1	2	3	2	52	33	17	3	44	19	2	74	1	79	49	25	2	1	5	3	8	5	2	8	4	0	60	1	0	0	41	21	12	6	1	58	1
145	318362	Cohort 2(Non CMV)	51	1	167	46	1.46	2	2	2	3	2	56	23	12	1	60	34	2	43	1	80	58	29	1	1	12	5	9	6	2	15	4	1	74	1	2	28	46	28	9	3	0	59	1
146	265617	Cohort 2(Non CMV)	56	2	158	54	1.53	2	2	3	3	1	76	18	6	2	43	29	1	45	1	76	49	25	2	1	11	3	8	4	1	11	5	1	67	1	2	28	46	27	8	5	0	75	1
147	327072	Cohort 2(Non CMV)	50	2	151	37	1.24	2	2	2	2	2	63	22	14	3	57	31	1	50	1	65	43	27	2	1	5	3	8	12	2	7	3	0	55	1	2	25	48	32	10	4	1	62	1
148	243950	Cohort 2(Non CMV)	50	2	156	37	1.26	2	2	2	2	1	55	20	13	1	38	28	2	50	1	74	48	23	2	1	12	4	12	15	1	11	5	1	66	1	2	26	36	24	8	3	0	73	1
149	328776	Cohort 2(Non CMV)	52	2	158	56	1.56	1	2	2	3	1	64	10	6	1	48	24	3	56	1	130	64	25	2	1	45	7	11	25	1	16	7	1	78	1	2	85	51	24	10	3	0	50	4
150	336619	Cohort 2(Non CMV)	60	1	168	65	1.74	2	2	2	3	2	74	29	16	2	49	30	2	34	1	102	68	27	2	1	5	3	8	10	2	12	4	0	62	1	0	31	47	28	18	4	0	61	1
151	321000	Cohort 2(Non CMV)	39	2	145	52	1.44	2	2	2	3	2	56	39	13	2	58	24	3	58	1	99	68	27	2	1	4	3	8	7	2	15	9	0	40	1	1	18	38	26	17	5	1	68	1
152	243436	Cohort 2(Non CMV)	30	1	161	43	1.38	2	2	2	3	2	74	30	15	1	34	20	2	57	2	71	49	25	1	1	7	4	8	10	1	15	9	1	65	1	2	28	43	31	111	3	1	65	1
153	334914	Cohort 2(Non CMV)	38	1	163	69	1.76	2	2	2	3	1	61	18	8	1	39	25	1	24	1	100	65	27	2	2	10	3	9	10	1	8	3	0	58	1	0	0	34	30	7	3	2	69	1
154	343254	Cohort 2(Non CMV)	56	2	158	52	1.51	2	2	2	3	2	60	35	26	3	62	20	3	60	1	80	58	27	2	2	11	4	10	10	2	10	5	1	66	1	2	32	29	20	14	4	1	59	1
155	255916	Cohort 2(Non CMV)	52	1	172	62	1.7	2	2	2	3	2	68	36	12	3	57	25	3	24	1	114	64	29	2	1	7	3	8	10	2	11	6	0	53	1	0	0	44	28	8	3	0	60	1
156	334560	Cohort 2(Non CMV)	49	2	160	64	1.68	2	2	2	2	2	73	22	16	3	63	27	2	31	1	66	43	29	2	1	6	3	8	5	2	16	7	1	72	1	3	31	70	25	14	4	0	56	1
157	313772	Cohort 2(Non CMV)	42	2	154	56	1.54	2	2	2	2	1	69	28	16	2	48	31	0	50	1	65	42	29	2	1	11	4	10	10	1	6	3	1	62	1	0	0	43	25	12	6	0	55	1
158	311949	Cohort 2(Non CMV)	42	2	156	72	1.76	2	2	2	2	1	70	24	13	1	36	27	3	63	1	103	64	25	2	1	5	4	10	10	1	8	2	0	55	1	0	0	31	22	13	6	0	63	1
159	339823	Cohort 2(Non CMV)	45	1	161	63.5	1.68	2	2	2	2	2	63	26	11	3	66	33	1	0	1	83	59	25	2	1	5.5	6	9	7	2	12	7	1	55	1	0	0	54	36	15	5	1	45	1
160	323579	Cohort 2(Non CMV)	28	1	163	60	1.64	2	2	2	1	1	74	41	23	1	58	26	2	65	1	64	47	25	2	2	6	4	8	5	1	18	5	0	67	1	2	25	44	30	14	4	1	64	1
161	335481	Cohort 2(Non CMV)	58	2	143	41	1.31	2	2	2	2	2	71	23	13	2	45	27	1	35	1	90	60	27	1	2	8	3	8	15	2	13	6	1	58	1	2	24	42	27	9	5	1	67	1
162	344810	Cohort 2(Non CMV)	47	2	159	62	1.65	2	1	2	2	1	58	26	17	2	50	22	1	75	1	77	50	23	2	1	7	3	8	5	1	8	4	0	43	1	1	20	47	20	12	5	1	55	1
163	269150	Cohort 2(Non CMV)	36	1	154	49	1.44	2	2	2	2	1	59	32	20	1	60	24	2	85	3	106	64	29	1	1	18	3	8	10	1	7	2	0	70	1	1	55	55	24	8.5	4	0	63	1
164	268628	Cohort 2(Non CMV)	25	1	170	62	1.71	2	2	2	2	1	73	28	15	3	55	27	0	0	2	143	97	29	1	2	56	7	9	15	1	9	3	1	60	2	0	0	47	34	13	4	2	72	1
165	268933	Cohort 2(Non CMV)	36	2	156	54	1.52	2	2	2	3	1	55	41	29	1	56	22	2	24	1	112	76	27	1	1	13	4	7	10	1	10	3	1	70	1	1	33	48	30	18	5	1	65	1
166	257882	Cohort 2(Non CMV)	55	2	144	47	1.37	2	2	2	3	1	54	17	10	2	46	22	1	0	1	77	47	27	2	1	15	4	10	10	2	5	2	1	43	1	0	0	34	29	6	2	0	75	1
167	239590	Cohort 2(Non CMV)	52	2	147	40	1.27	2	2	2	3	2	65	50	20	3	57	26	3	44	1	104	69	27	2	2	14	4	8	15	2	9	3	0	63	1	2	22	35	28	15	6	1	74	1
168	246006	Cohort 2(Non CMV)	33	2	152	61	1.8	2	2	2	2	1	68	37	28	1	46	24	1	48	1	92	63	27	2	2	10	3	8	10	1	9	3	0	60	1	1	23	22	20	12	6	0	65	1
169	9403612	Cohort 2(Non CMV)	38	2	151	63	1.62	2	2	2	3	2	58	32	13	3	59	22	2	41	1	96	61	27	2	1	17	3	11	20	2	14	5	0	80	1	3	30	49	23	21	7	0	70	1
170	251699	Cohort 2(Non CMV)	19	2	147	46	1.37	2	2	2	3	2	50	25	17	1	52	28	3	68	1	84	56	31	2	1	17	4	7	10	2	6	2	1	56	1	3	29	39	27	16	5	0	72	1
171	9005629	Cohort 2(Non CMV)	34	1	166	66	1.75	2	2	2	2	1	62	37	24	2	52	27	2	58	1	93	65	27	2	1	6	3	8	5	1	6	3	0											

TR 4	RVSP 4	LA4	AORTA 4	MS GR PK5	MS GR MEAN 5	MR 5	EF5	RVF 5	TR 5	RVSP 5	LAS	AORTA 5	D/S TO CMV	CMV TOSX	Duration toSX
2	22	33	24	9	3	2	62	1	0	0	36	25	3	26	0
2	30	52	32	13	4	2	28	4	2	35	46	28	3	22	0
2	30	84	32	8	3	1	56	2	1	36	74	30	1	18	0
0	0	45	32	9	2	1	54	1	1	0	38	27	3	13	0
2	32	52	29	17	6	0	64	1	3	55	51	37	2	25	0
3	30	61	31	18	8	1	64	1	1	33	46	34	2	17	0
1	0	42	28	13	6	0	65	1	1	0	42	30	3	13	0
3	20	51	24	14	6	1	57	1	3	20	51	37	14	15	0
2	22	37	30	11	6	0	59	1	2	35	47	29	18	19	0
2	36	49	30	16	8	0	69	1	1	38	50	25	9	17	0
3	38	33	27	8	6	1	50	1	1	40	36	21	3	34	0
2	30	40	20	11	6	0	55	1	0	0	35	27	2	21	0
2	38	40	28	13	4	2	80	1	2	16	42	21	4	21	0
1	0	53	39	10	4	1	35	1	0	0	50	35	3	37	0
0	0	41	35	19	4	0	66	1	2	24	40	25	3	17	0
1	0	40	24	7	2	1	61	1	2	30	36	26	13	26	0
0	0	38	27	13	6	1	63	1	0	0	53	34	15	14	0
0	42	34	28	9	5	1	65	1	1	16	36	24	10	20	0
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3	30	62	32	16	6	1	65	2	3	34	70	29	3	22	0
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Plagiarism Checker X Originality Report

Similarity Found: 0%

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Statistics: 0 words Plagiarized / 563 Total words

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