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# OUTCOMES AND PREDICTORS OF IN-HOSPITAL MORTALITY IN INFECTIVE ENDOCARDITIS PATIENTS REQUIRING SURGERY

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# INTRODUCTION

- Despite the advances in technology and surgery, Infective endocarditis (IE) remains a disease with significant mortality and morbidity
  - 15-30% in-hospital mortality
- Proportion of IE cases undergoing valve surgery increased 7% per decade between 1970 to 2000
- Surgery gives a **survival advantage of up to 20% in the first year**
- 3 main indications of surgery :
  - Heart failure
  - Uncontrolled infection
  - Embolism prevention

# OBJECTIVES

## 01 General Objective

1. To evaluate the clinical outcomes of IE in adult patients requiring surgery
2. To determine the significant predictors associated with in-hospital mortality.

## 02 Specific Objectives

1. To determine the association of the demographic, echocardiographic, microbiological findings, surgical procedure, pre-and-post operative complications, reasons for not proceed surgery with hospitalization outcomes.
2. To identify predictors for all-cause in-hospital mortality during admissions of new, relapse or recurrent cases.
3. To determine long term all-cause mortality

# STUDY POINTS / OUTCOMES

## 01 Primary Endpoint

- All-cause in-hospital mortality

## 02 Secondary Endpoints

- Pre-and-post-operative complications.
- Long term all-cause mortality

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# STUDY METHOD

- A single centre, retrospective observational study
- Period between January 2018 – December 2022
- Cardiac tertiary center of National Heart Institute, Kuala Lumpur, Malaysia
- Patients registered under local Infective Endocarditis (IE) Registry
- Maximum follow up duration: 60 months

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# STUDY CRITERIA

## 01 Inclusion Criteria

(1) Acute, recurrent and relapsed IE

(2) IE with least one valve infected or mixed with cardiac implantable electronic devices or congenital heart disease related infection.

(3) IE referred for valvular surgery within the readmission.

## 02 Exclusion Criteria

(1) Patients age below 18 (Paediatric cases)

(2) IE, treated as outpatient visit (resolved IE)

(3) Cardiac implantable electronic devices or congenital heart disease related infection only.

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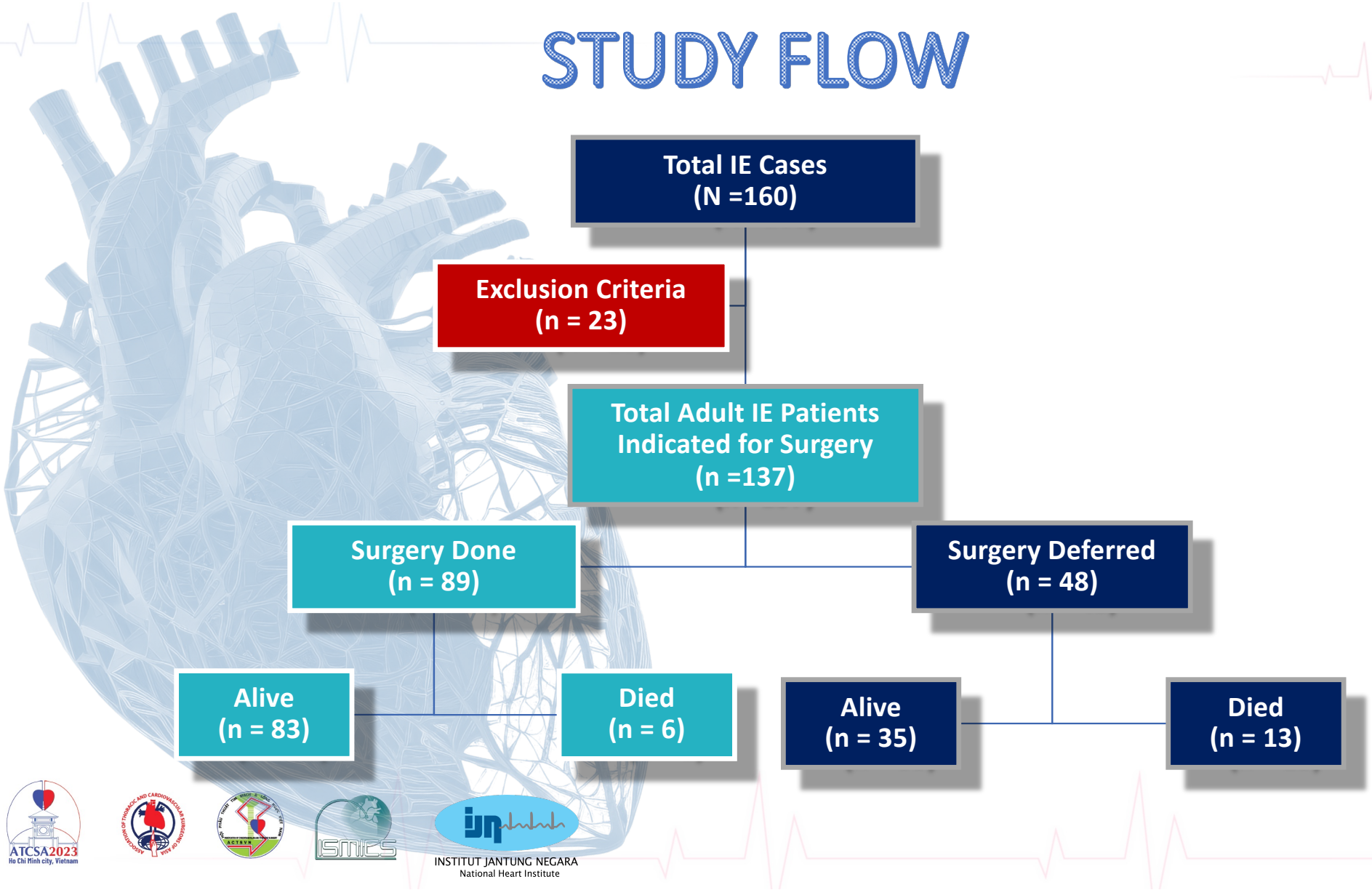
# STUDY FLOW

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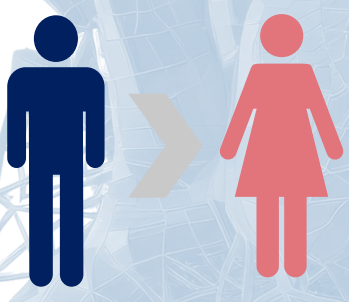
# DEMOGRAPHIC

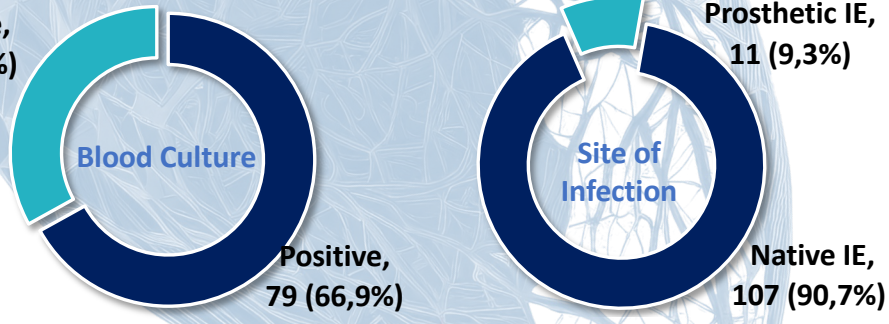
**TOTAL IE PATIENTS : 137**

## Alive ; n = 118

**68.6%** (n = 81) — **31.4%** (n = 37)

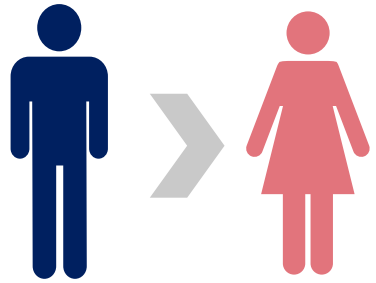


**Age at Admission**
Mean (SD) : 45.7 (15.2)
Median (Q1, Q3) : 47.9 (31.8, 58.0)

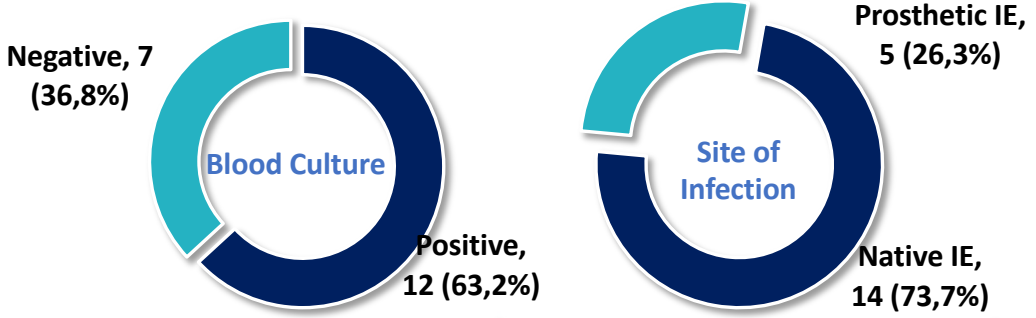



## Died ; n = 19

**78.2%** (n = 15) — **21.1%** (n = 4)



**Age at Admission**
Mean (SD) : 57.1 (16.5)
Median (Q1, Q3) : 60.5 (39.8, 68.5)




**SIGNIFICANT** DIFFERENCE IN AGE OF ADMISSION

P=0.003

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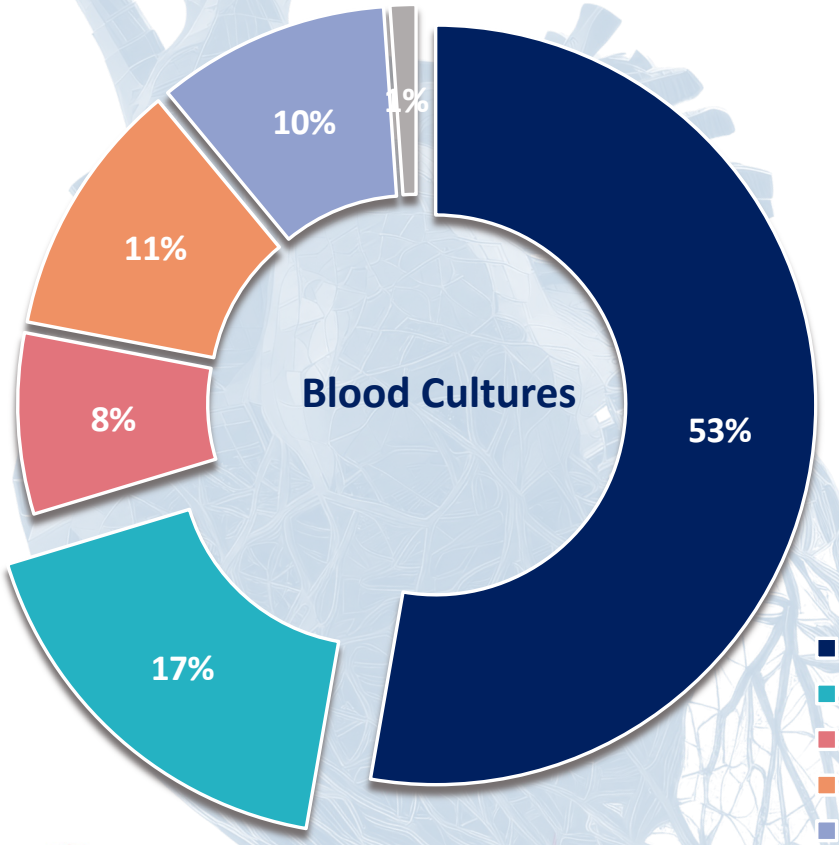
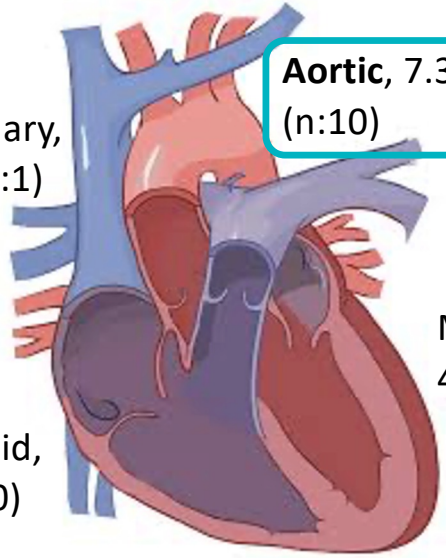
# MICROBIOLOGY




| ORGANISM | TOTAL (n =91) | ALIVE | DEAD | P - VALUE |
|---|---|---|---|---|
| Staph Aureus | 16 (17.6%) | 12 (15.2%) | 4 (33.3%) | 0.213 |
| Non-Staph Aureus | 75 (82.4%) | 67 (84.8%) | 8 (66.7%) | |

# VALVULAR INVOLVEMENT

## Prosthetic



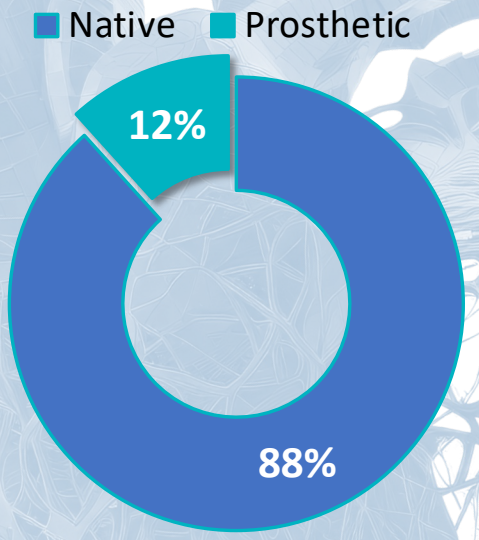
**Aortic**, 7.3% (n:10)

Pulmonary, 0.7% (n:1)

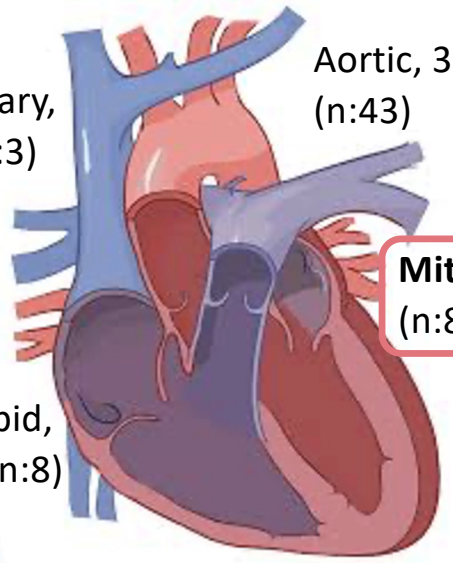
Mitral, 4.4% (n:6)

Tricuspid, 0% (n:0)

n : 16




## Native



Pulmonary, 2.2% (n:3)

Aortic, 31.4% (n:43)

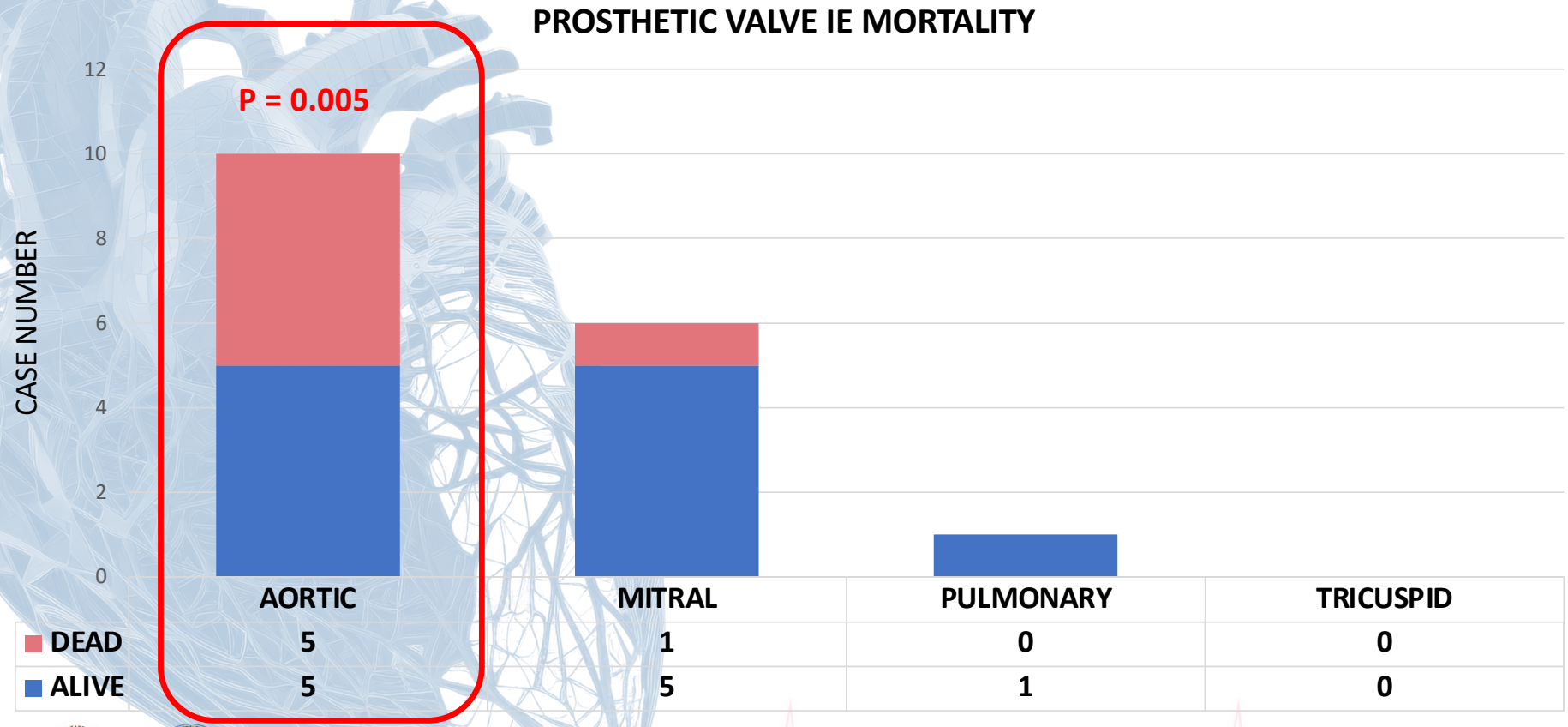
**Mitral**, 62.% (n:85)

Tricuspid, 5.8% (n:8)

n : 121

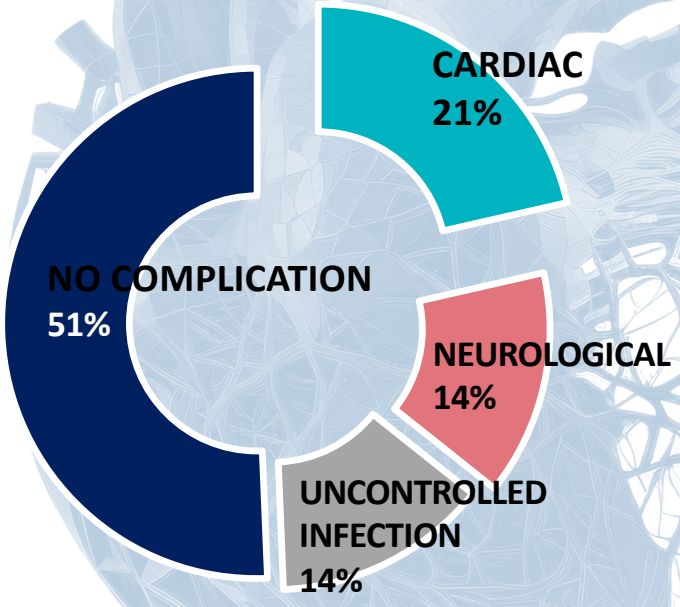
Mortality in **PVE** is **31.3%** (5/16) VS Mortality in **NVE** is **11.5%** (14/121)
**(P = 0.048)**

# PROSTHETIC IE AND MORTALITY




| | AORTIC | MITRAL | PULMONARY | TRICUSPID |
|---|---|---|---|---|
| DEAD | 5 | 1 | 0 | 0 |
| ALIVE | 5 | 5 | 1 | 0 |

# PRE-OPERATIVE IE COMPLICATIONS




| COMPLICATIONS | ALIVE (n = 116) | DEAD (n = 21) | P-VALUE |
|---|---|---|---|
| **No complications** | **72 (62.0%)** | **6 (31.6%)** | **0.016** |
| **Presence of complications** | **44 (38.0%)** | **15 (68.4%)** | |

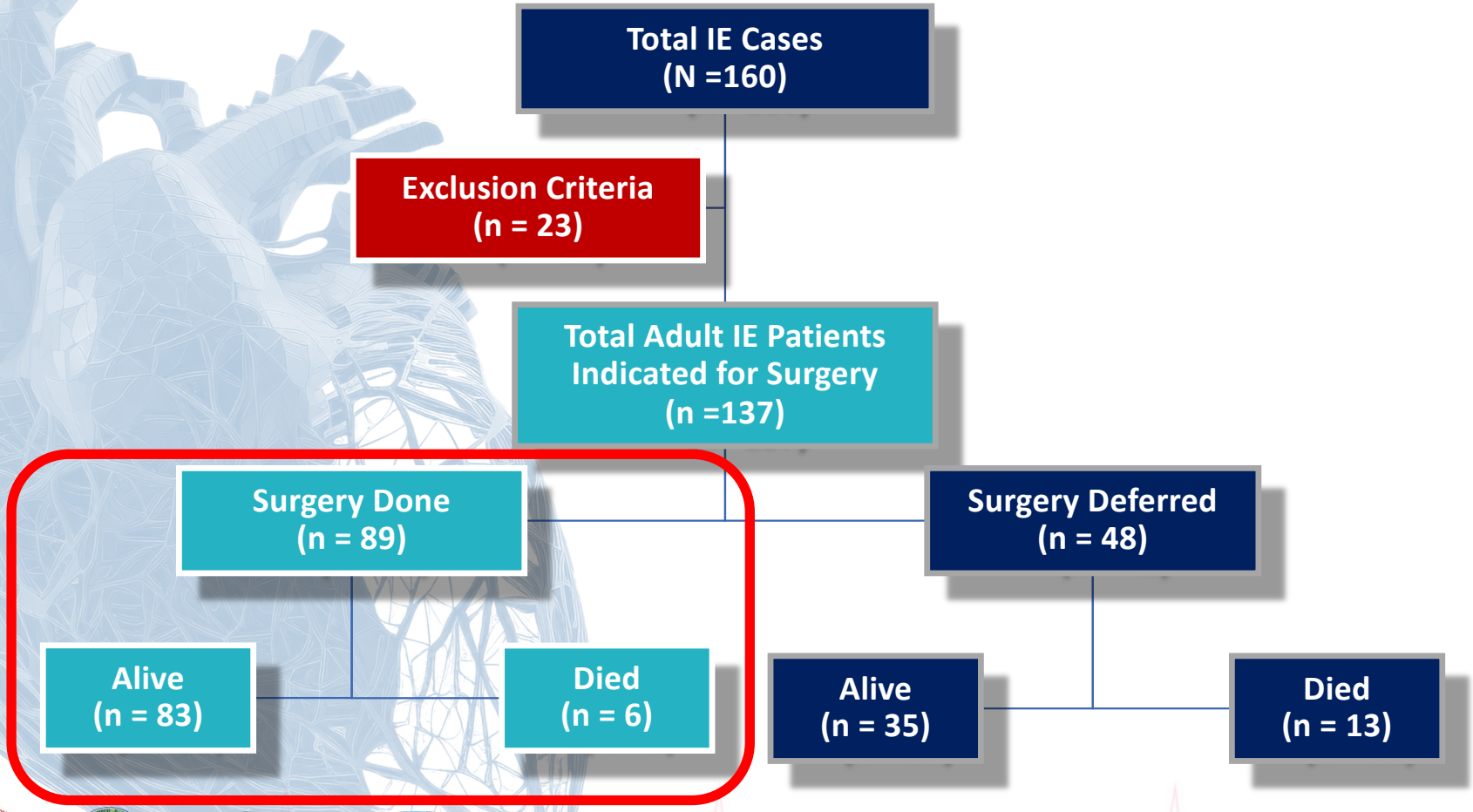
| CARDIAC COMPLICATIONS | ALIVE (n = 116) | DEAD (n = 21) | P-VALUE |
|---|---|---|---|
| **Cardiogenic shock** | **2 (1.7%)** | **6 (31.6%)** | **<0.001** |
| **Congestive heart failure** | **20 (16.9%)** | **8 (42.1%)** | **0.027** |
| **New conduction abnormality** | **2 (1.7%)** | **3 (15.8%)** | **0.019** |
| Intracardiac abscess | 0 | 1 (5.3%) | 0.139 |

| NEUROLOGICAL COMPLICATIONS | ALIVE (n = 116) | DEAD (n = 21) | P-VALUE |
|---|---|---|---|
| Embolic stroke | 10 (8.5%) | 4 (21.1%) | 0.107 |
| Haemorrhagic stroke | 8 (6.8%) | 0 | 0.599 |
| Mycotic aneurysm | 5 (4.2%) | 0 | 1.000 |
| Meningitis / Encephalitis / Abscess | 1 (0.8%) | 0 | 1.000 |

# INDICATION FOR SURGERY

| INDICATION | TOTAL, n (%) | ALIVE, n (%) | DEAD, n (%) | P-VALUE |
|---|---|---|---|---|
| **Uncontrolled heart failure** | **25 (18.2)** | **18 (15.3)** | **7 (36.8)** | **0.026** |
| **Hemodynamic instability** | **7 (5.1)** | **0** | **7 (36.8)** | **<0.001** |
| Uncontrolled sepsis | 17 (12.4) | 12 (10.2) | 5 (26.3) | 0.062 |
| Vegetations | 71 (51.8) | 62 (52.5) | 9 (47.4) | 0.675 |
| Paravalvular involvement | 6 (4.4) | 4 (3.4) | 2 (10.5) | 0.195 |
| Valve dehiscence | 3 (2.2) | 3 (2.5) | 0 | 1.000 |
| **Valvular regurgitation** | **111 (81.0)** | 96 (81.4) | 15 (78.9) | 0.759 |
| Embolisation | 23 (16.8) | 18 (15.3) | 5 (26.3) | 0.317 |
| Myocardial abscess | 1 (0.7) | 1 (0.8) | 0 | 1.000 |
| Other surgical indication | 2 (1.5) | 2 (1.7) | 0 | 1.000 |

# SURGICAL COHORT SUB ANALYSIS

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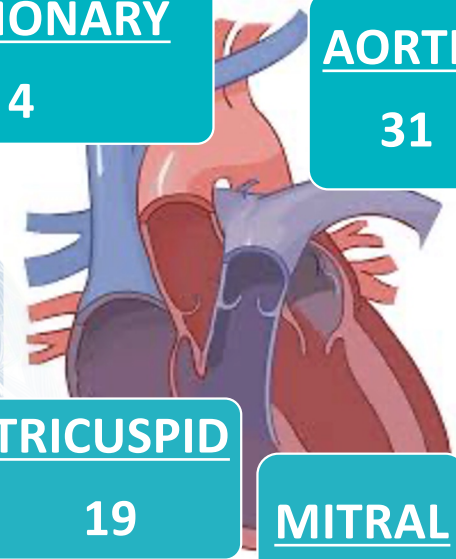
# SURGICAL COHORT : VALVULAR INTERVENTION



**PULMONARY**
4

- BIOPROSTHETIC 2
- REPLACE 2
- REPAIR 2

**AORTIC**
31

- REPLACE 31
  - MECHANICAL : 27
  - BIOPROSTHETIC : 4
- REPAIR 0

**TRICUSPID**
19

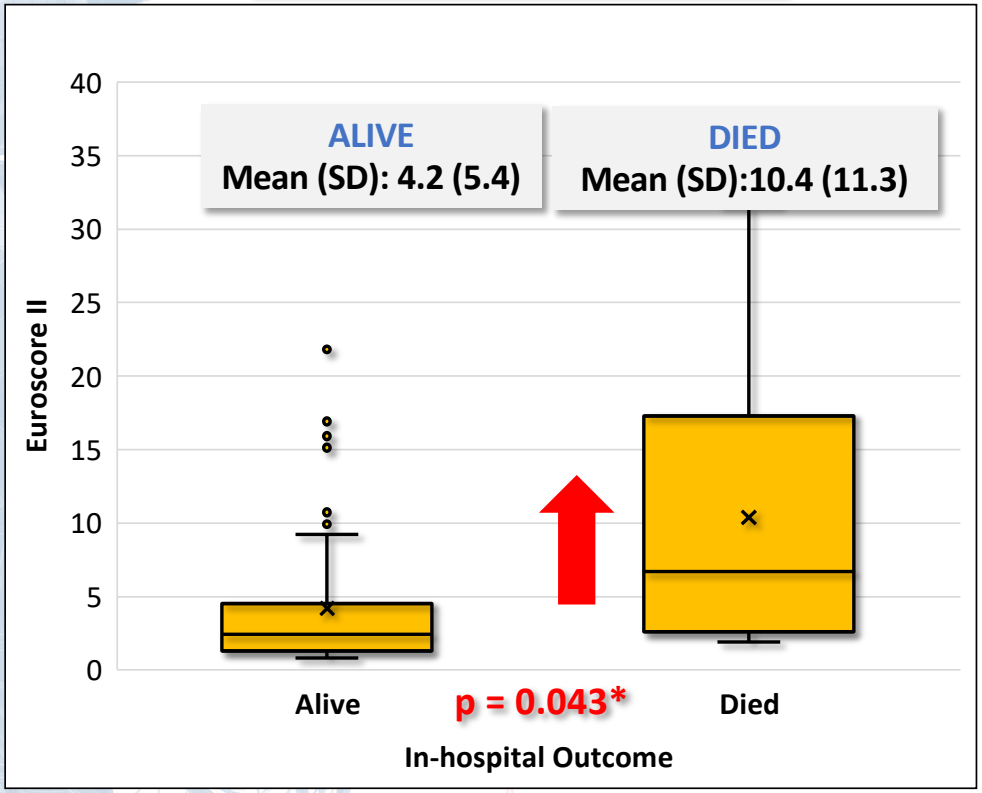
- REPLACE 2
  - MECHANICAL : 0
  - BIOPROSTHETIC : 2
- REPAIR 17
  - RING : 9
  - DE VEGA : 6
  - NEOCHORDAE : 1

**MITRAL**
61

- REPLACE 50
  - MECHANICAL : 40
  - BIOPROSTHETIC : 10
- REPAIR 11
  - RING : 10
  - NEOCHORDAE : 1

# SURGICAL COHORT : EUROSCORE

## EuroScore II

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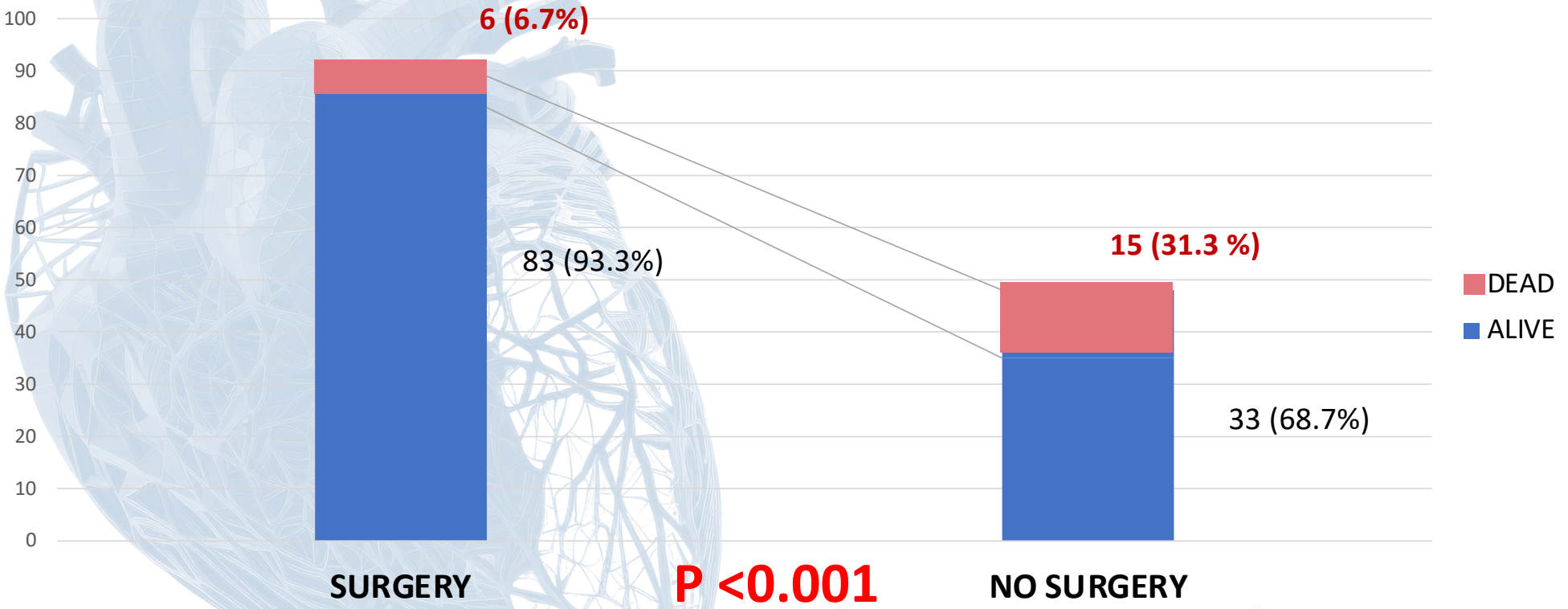
# SURGICAL COHORT : COMPARATIVE ANALYSIS

| VARIABLE, mean (SD) | ALIVE | DIED | P-VALUE |
|---|---|---|---|
| LVEF (%) | 57.6 (8.7) | 53.5 (9.3) | 0.253 |
| CPB time (min) | 129.9 | 181.8 (87.5) | 0.099 |
| X Clamp time (min) | 97.7 (46.4) | 125.7 (58.2) | 0.197 |
| Post op LOS (days) | 13.4 (8.7) | 9.8 (5.3) | 0.583 |

Overall, **NO clinical significance** between the two cohort

# MORTALITY RATE



# SURGICAL COHORT : POST OP COMPLICATIONS

| COMPLICATIONS | TOTAL | ALIVE | DEAD | P-VALUE |
|---|---|---|---|---|
| **Neurological** | 5 (5.6) | 3 (3.6) | 2 (33.3) | **0.035** |
| **Heart failure** | 6 (6.7) | 2 (2.4) | 4 (66.7) | **<0.001** |
| **Renal failure** | 3 (3.4) | 1 (1.2) | 2 (33.3) | **0.011** |
| **Prolonged ventilation** | 4 (4.5) | 2 (2.4) | 2 (33.3) | **0.022** |
| Bleeding requiring reopen | 3 (3.4) | 2 (2.4) | 1 (1.67) | 0.191 |
| Reinfection of new valve | 1 (1.1) | 1 (1.2) | 0 | 1.000 |
| Others | 11 (12.4) | 10 (12.0) | 1 (16.7) | 0.558 |

# PREDICTORS OF IN-HOSPITAL MORTALITY

| Variables | Univariate Log Regression 95% CI | | | |
|---|---|---|---|---|
| | Unadjusted OR | Lower | Upper | p-value |
| Age | 1.052 | 1.015 | 1.090 | 0.006 |
| NYHA III-IV | 3.430 | 1.166 | 10.090 | 0.025 |
| History of prosthetic valve implant | 3.474 | 1.052 | 11.476 | 0.041 |
| Prosthetic valve infection | 3.474 | 1.052 | 11.476 | 0.041 |
| Absence of pre-op IE Complication | 0.295 | 0.105 | 0.831 | 0.021 |
| IE with Cardiogenic shock | 26.769 | 4.891 | 146.515 | <0.001 |
| IE with Congestive heart failure | 3.564 | 1.272 | 9.981 | 0.016 |
| IE New conduction abnormality | 10.875 | 1.686 | 70.137 | 0.011 |
| Surgical candidate with uncontrolled heart failure | 3.241 | 1.124 | 9.41 | 0.029 |
| Deferred surgery | 5.138 | 1.807 | 14.608 | 0.002 |

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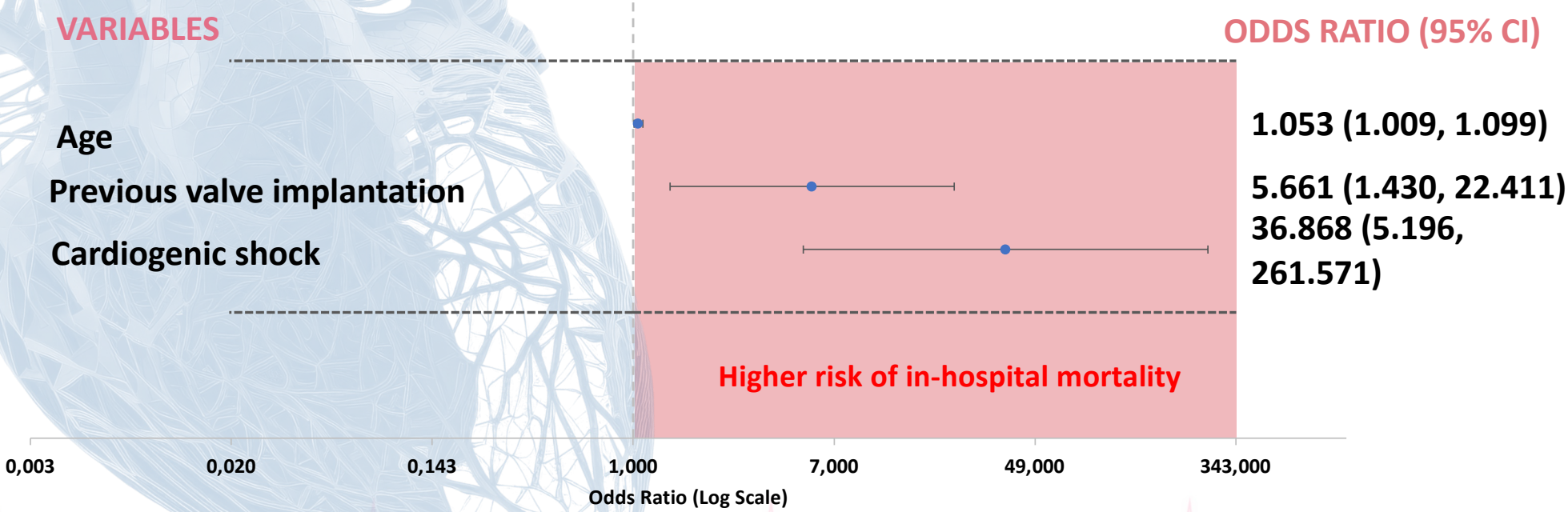
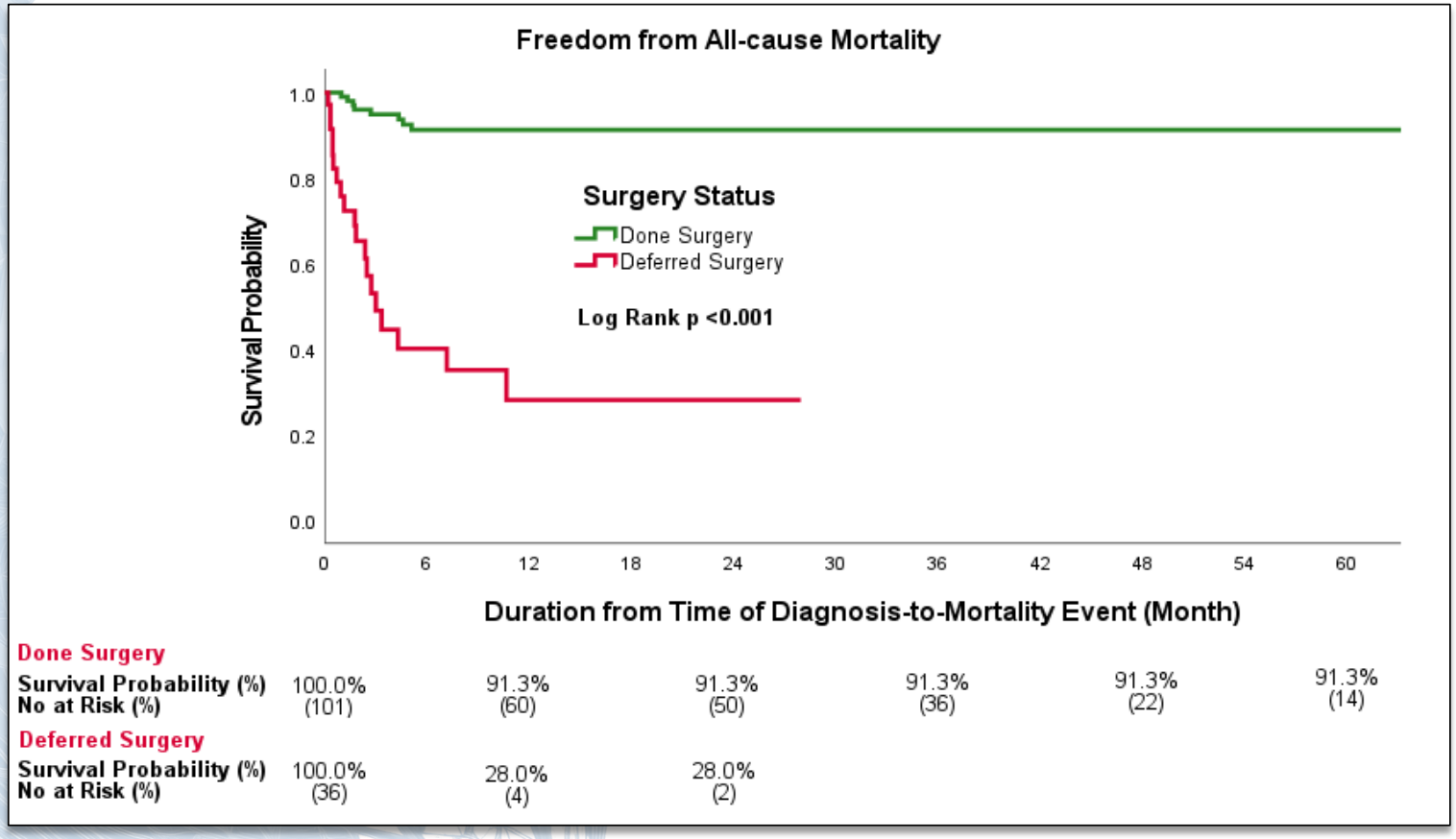
# INDEPENDENT PREDICTORS OF IN-HOSPITAL MORTALITY

**Predictors of In-hospital Mortality among Adult Patients with Infective Endocarditis Indicated for Surgery**



# SURVIVAL ANALYSIS




| | | | | | | |
|---|---|---|---|---|---|---|
| **Done Surgery** | | | | | | |
| **Survival Probability (%)** | 100.0% | 91.3% | 91.3% | 91.3% | 91.3% | 91.3% |
| **No at Risk (%)** | (101) | (60) | (50) | (36) | (22) | (14) |
| **Deferred Surgery** | | | | | | |
| **Survival Probability (%)** | 100.0% | 28.0% | 28.0% | | | |
| **No at Risk (%)** | (36) | (4) | (2) | | | |

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# DISCUSSION

- Overall in-hospital mortality is 13.9%
  - Guiomar et al 13.1%, Moreira et al 15% and Farag et al 18.3%
- PVE in-hospital mortality is **31.3%** (5/16) vs **11.5%** (14/121)
  - ESC IE guideline quoted 20-40% in-hospital PVE mortality
- 3 independent predictors of mortality identified :
  - Cardiogenic shock
  - Previous valvular implantation
  - Advanced age
- Other predictors of mortality includes : NYHA III-IV, Absence of pre-op IE complication, congestive heart failure and deferred surgery
- Most of the predictors consistent with other predictors as per ESC guideline

# DISCUSSION

- Surgery is a protective factor against mortality
- Surgery was associated with significant reduction in in-hospital mortality (6.7% vs 31.3%, p <0.001) as compared to :
  - Moreira et al (15.5% vs 32.6%, p = 0.028)
  - Lalani et al (12.1% vs 20.7%, p<0.001)
- Excellent post-operative survival for IE in our cohort is 91.3% over 5 years as opposed to Farag et al (63.3% post op survival over 5 years)

# LIMITATIONS

- Small, granular data
- Single cardiac center
- Retrospective, observational study – Prone to Survival Bias
- Referral from other centre – Difficult to assess the timing of surgery
- Only up to 5 years follow up – Longer duration of follow up allows us to look into long term mortality

# CONCLUSIONS

- Surgical intervention reduces mortality
- Independent predictors of in-hospital mortality for IE were **cardiogenic shock**, **previous valvular implantation** and **age**
- Predictors of all-cause in-hospital mortality also includes **preoperative heart failure**, **new conduction** abnormality and **deferred surgery.**
- **Significantly higher PVE mortality** emphasize the importance of prevention and prompt treatment of PVE.
- Early identification of patients with strong predictors of mortality may be helpful in improving outcome.

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# THANK YOU

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# APPENDIX: STATISTICAL ANALYSIS

## 01 Descriptive Analysis

- Continuous variables : mean with standard deviations / median with interquartile range (IQR)
- Categorical variables : percentages

## 02 Comparative Analysis

- Continuous variables : independent t-test or Mann Whitney test
- Categorical variables : chi-square test or Fisher's exact test

## 03 Predictive Analysis

Logistic regression :

- Univariate analysis ($p<0.05$) were included in the multivariate analysis with a forward Likelihood Ratio (LR) stepwise approach.
- Results :
  - unadjusted odds ratios (un-aOR)
  - adjusted odds ratios (aOR) with 95% (95% CIs).

## 04 Survival Analysis

- Kaplan-Meier method