



Article History:

Received: 09-02-2025 Accepted: 26-03-2025 Publication: 03-04-2025

Cite this article as:

Lee, J.-S., Sales, L., Moter, A., & Eichinger, W. (2025). Impact of the COVID-19 Pandemic on Surgical Outcomes of Native and Prosthetic Valve Endocarditis: A Retrospective Subanalysis. *Journal of Heart Valve Disease Innovation*, 30(1). 28-37. doi.org/10.36923/jhvd.v30i1.255

©2025 by author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License 4.0 International License.

Corresponding Author(s):

Jang-Sun Lee

Department of Cardiac Surgery Kerckhoff Heart Center, Bad Nauheim Benekestrasse 2-8, D-61231 Bad Nauheim, Germany. Email: j.lee@kerckhoff-klinik.de

Impact of the COVID-19 Pandemic on Surgical Outcomes of Native and Prosthetic Valve Endocarditis: A Retrospective Subanalysis

Jang-Sun Lee¹, Virna L. Sales², Annette Moter³, Walter Eichinger⁴

Abstract: Background and aim of the study: During the COVID-19 pandemic in Bavaria, surgical ICU resources were reallocated, and elective procedures were postponed, impacting the management of infective endocarditis (IE). This study evaluated early surgical outcomes in patients with native valve endocarditis (NVE) and prosthetic valve endocarditis (PVE) before and during the pandemic. Methods: We retrospectively analyzed 94 patients (66% male) treated pre-pandemic (August 2018-March 21, 2020) and 84 patients (76% male) treated during the pandemic (March 22, 2020-November 2021). NVE cases comprised 78% pre-pandemic and 68% during the pandemic, while PVE cases increased from 22% to 32%. Preoperative characteristics, surgical urgency, postoperative complications, and in-hospital mortality were assessed. Explanted valves underwent histological, microbiological, and molecular analyses, including fluorescence in situ hybridization (FISH) with 16S rRNA PCR/sequencing. Results: During the pandemic, preoperative NYHA class III-IV increased significantly (NVE: 49% to 74%; PVE: 29% to 70%; all p<0.05). Urgent surgeries became more frequent (NVE: 27% to 49%, p=0.017; PVE: 20% to 52%, p=0.034), and the interval from diagnosis to surgery in PVE patients was prolonged (11 vs. 16 days, p=0.038). More complex procedures, including double-valve surgeries, were required (9.5% vs. 37%, p=0.022). Postoperatively, rethoracotomy rates increased in NVE cases (OR: 9.106, p<0.001), while odds ratios for stroke, sepsis, and prolonged ICU stay in PVE patients trended higher but lacked statistical significance. Conclusion: The pandemic led to diagnostic delays, worsened preoperative conditions, and increased surgical urgency in IE patients, underscoring the need for resilient healthcare strategies to maintain timely surgical care during future crises.

Keywords: Endocarditis, Prosthetic Valve Endocarditis, Re-do Surgery, COVID-19, FISH

1. Introduction

The COVID-19 pandemic necessitated the implementation of strict lockdown measures worldwide, including the temporary suspension of non-elective surgeries to prioritize care for patients with COVID-19. Resources were reallocated, with intensive care unit (ICU) beds, ventilators, and ECMO devices redirected to meet the surge in demand. Our institution, a major municipal tertiary hospital in Munich, adhered to directives from the Bavarian government, focusing on the care of critically ill COVID-19 patients. While these measures were crucial, they significantly impacted surgical services, particularly cardiac surgery, which relies heavily on ICU resources and timely intervention for patients with deteriorating conditions (Ad et al., 2021; Hunger et al., 2022; J.-S. Lee et al., 2024).

Native valve endocarditis (NVE) is a life-threatening condition with high rates of in-hospital and surgical mortality. Early diagnosis, appropriate antibiotic therapy, and the optimal timing of surgery remain challenging despite advancements in antibiotic stewardship, actual guidelines, and the collaborative efforts of Heart Teams (Baddour et al., 2015; Delahaye et al., 2007; Delgado et al., 2023). Conversely, prosthetic valve endocarditis (PVE), with an annual incidence of 0.3–1.2% per patient, presents diagnostic difficulties due to non-specific symptoms and imaging artifacts, particularly on transthoracic echocardiography (Ivanovic et al., 2019; Lalani et al., 2013).

This study aimed to analyze the preoperative and postoperative outcomes of patients with NVE and PVE before and during the COVID-19 pandemic, highlighting the impact of pandemic-related healthcare disruptions on these high-risk surgical cohorts.

¹ Department of Cardiac Surgery, Munich Hospital Bogenhausen, Munich, Germany, Technical University Munich, Munich, Germany

¹Department of Cardiac Surgery, Kerckhoff Clinic, Bad Nauheim, Germany, University Hospital of Giessen, Giessen, Germany

² Department of Cardiac Surgery, Munich Hospital Bogenhausen, Munich, Germany, Technical University Munich, Munich, Germany

² Department of Cardiology, Angiology, and Medical Intensive Care, Cardiovascular Center of Hersfeld-Rothenburg, Germany

³ Institute of Medical Microbiology and Epidemiology of Infectious Disease, University Hospital of Leipzig, Leipzig, Germany

³ Biofilmcenter at the German Heart Institute Berlin, University of Charité, Berlin, Germany

³ MoKi Analytics GmbH, Berlin, Germany

³ Moter Diagnostics, Berlin, Germany

⁴ Department of Cardiac Surgery, Munich Hospital Bogenhausen, Munich, Germany, Technical University Munich, Munich, Germany

2. Patients and methods

This retrospective subanalysis involved 178 adult patients who underwent cardiac surgery and received postoperative antibiotic therapy for infective endocarditis (IE) between August 2018 and November 2021. The patients were categorized into two main cohorts: native valve endocarditis (NVE, n = 130) and prosthetic valve endocarditis (PVE, n = 48). Each cohort was further subdivided based on the period of surgery: pre-pandemic (August 2018 to March 21, 2020; NVE: 73 patients, PVE: 21 patients) and pandemic (March 22, 2020 to November 2021; NVE: 57 patients, PVE: 27 patients). All surgical interventions were performed following confirmation of a negative COVID-19 test.

Data for this study were extracted from the Cardiac Surgery Outcomes Registry, a dataset approved by the Institutional Review Board. This registry captures comprehensive preoperative, perioperative, and early postoperative outcomes and adheres to the standards of the Institute for Quality Assurance and Transparency in Health Care (https://iqtig.org). We also analyzed the time intervals between symptom onset and diagnosis, as well as from diagnosis to surgery, for all cohorts.

Comorbidities were classified according to the Society of Thoracic Surgeons (STS) National Database criteria (www.sts.org). These included the New York Heart Association (NYHA) functional classification and the Canadian Cardiovascular Society (CCS) angina grading system. Cardiac surgeries were performed with cardiopulmonary bypass (CPB), utilizing crystalloid cardioplegia for myocardial protection.

The diagnosis of postoperative IE was established using the modified Duke criteria and intraoperative findings. Intraoperative assessments included histopathological and microbiological evaluations, alongside fluorescence in situ hybridization (FISHseq) analysis. The FISHseq procedure was selectively employed based on preoperative and intraoperative findings and involved the resection of suspicious native or prosthetic valve tissue. Tissue samples were prepared and sent to MoKi Analytics GmbH and Moter Diagnostics in Berlin for FISHseq analysis. This methodology, as described by Eichinger et al., is recognized as a definitive pathological criterion under the 2023 Duke–International Society for Cardiovascular Infectious Diseases (ISCVID) guidelines (Eichinger et al., 2019). Patients who did not meet Duke criteria or showed no intraoperative evidence of IE were excluded from the analysis (Figure 1).

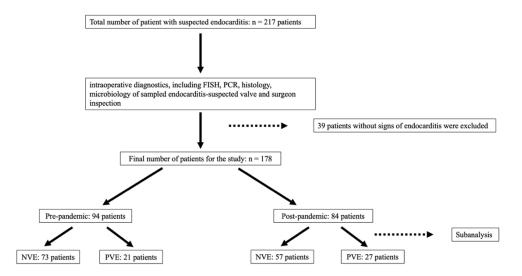


Figure 1: Flowchart of study design. A diagram illustrating the study's methodology, patient inclusion criteria, and division into pre- and post-pandemic cohorts.

Postoperative complications were evaluated, including re-thoracotomy for bleeding, tracheotomy necessitated by prolonged mechanical ventilation, delirium, acute renal failure requiring dialysis, stroke, sepsis, and in-hospital mortality. Patient survival was confirmed through communication with primary care physicians or rehabilitation centers.

3. Statistical Analysis

Demographic characteristics, preoperative cardiac status, surgical details, pathogens, IE diagnostics, and in-hospital outcomes were compared between the subgroups undergoing elective or urgent/emergent surgeries. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized as means \pm standard deviation (SD). Group comparisons employed t-tests for normally distributed variables and Fisher's exact test for categorical data. Odds ratios (OR) with 95% confidence intervals were calculated. A p-value < 0.05 was considered statistically significant. Analyses were performed using SPSS (Version 29.0.1.0, IBM, Armonk, NY, USA), and visualizations, including boxplots, were created using R (Version 2023.06.1+524).

4. Results

4.1 Patient Characteristics: NVE

A total of 130 patients with native valve endocarditis (NVE) were included in this retrospective study. The gender distribution between the pre-pandemic and post-pandemic cohorts showed no significant difference (male: 51/73 vs. 43/75, p = 0.556), and the mean age was comparable (62.9 ± 12.9 vs. 64.3 ± 15.5 years, p = 0.341). However, the post-pandemic cohort exhibited a higher prevalence of NYHA functional class IV (13% vs. 18%, p = 0.018), alongside an increase in urgent surgeries (27% vs. 49%) and a decrease in elective surgeries (64% vs. 46%; all p < 0.05).

The time interval from symptom onset to diagnosis was longer in the post-pandemic cohort compared to the pre-pandemic cohort (9 days vs. 15 days), although this difference was not statistically significant (p = 0.884) (Figure 2.1). Other comorbidities, including left ventricular ejection fraction (LVEF), did not differ significantly between cohorts (Table 1). Coronary artery disease and Canadian Cardiovascular Society (CCS) angina classification, which influence LVEF, also showed no significant differences.

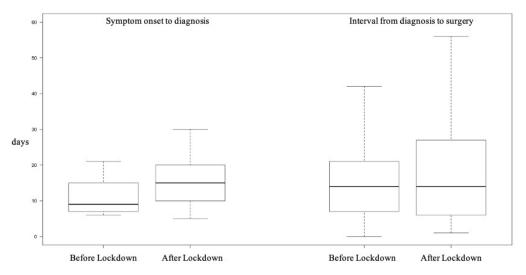


Figure 2: Time intervals from symptom onset to diagnosis and diagnosis to surgery in the NVE Cohort. Boxplots showing the time delays for the NVE cohort, comparing pre- and post-pandemic groups.

Table 1: Demographic and preoperative clinical characteristics of the NVE cohort (N=130).

| | 8/18 - 3/21/20 | 3/22/20 - 11/21 | |
|-------------------------|-----------------|--------------------|---------|
| | Before Lockdown | | D volue |
| | Nr./Mean (%) | After Lockdown | P-value |
| Cohort | 73 | Nr./Mean (%) 57 | |
| | 62.9 ± 12.9 | | 0.341 |
| Age | | 64.3 ± 15.5 | |
| Male | 51 (70) | 43 (75) | 0.556 |
| BMI | 26.4 ± 6.5 | 25.9 ± 5 | 0.964 |
| Creatinine (mg/dl) | 1.3 ± 1 | 1.3 ± 0.8 | 0.785 |
| Sinus rhythm | 62 (85) | 46 (81) | 0.639 |
| LV EF < 50% | 23 (32) | 6 (11) | 0.005 |
| COPD | 9 (12) | 8 (14) | 0.798 |
| Arterial hypertension | 29 (40) | 26 (46) | 0.592 |
| Diabetes mellitus | | | 0.371 |
| No therapy | 2 (3) | 5 (9) | 0.239 |
| Oral medication | 6 (8) | 3 (5) | 0.731 |
| Insulin therapy | 6 (8) | 3 (5) | 0.731 |
| Hyperlipidemia | 17 (23) | 16 (28) | 0.549 |
| Nicotine abuse | 11 (15) | 7 (12) | 0.799 |
| Alcohol abuse | 2 (3) | 0 | 0.504 |
| Family disposition | 0 | 2 (4) | 0.190 |
| Coronary Artery Disease | 25 (44) | 27 (47) | 0.151 |
| CCS | | | 0.915 |
| I | 67 (93) | 52 (90) | 1.000 |
| II | 4 (5) | 2 (4) | 0.695 |
| III | 1 (1) | 1 (2) | 1.000 |
| IV | 1 (1) | 2 (4) | 0.581 |
| NYHA | · / | · / | 0.012 |

| I | 16 (22) | 4 (7) | 0.026 |
|-------------------------------------|-------------------------------|----------------------------|---------------|
| II | 21 (29) | 11 (19) | 0.227 |
| III | 26 (36) | 24 (42) | 0.473 |
| IV | 10 (13) | 18 (32) | 0.018 |
| Rankin | | | 0.262 |
| No significant disability | 11 (15) | 12 (21) | 0.488 |
| Slight disability | 0 | 2 (4) | 0.190 |
| Moderate disability | 3 (4) | 1 (2) | 1.000 |
| Modified Duke | | | 0.122 |
| Definite | 53 (73) | 49 (86) | 0.086 |
| Possible | 14 (19) | 4 (7) | 0.071 |
| rejected | 6 (8) | 4 (7) | 1.000 |
| IE valve position | | | |
| Aortic valve | 41 (56.2) | 22 (38.6) | 0.053 |
| Mitral valve | 29 (39.7) | 22 (38.6) | 1.000 |
| Tricuspid valve | 1 (1.4) | 3 (5.3) | 0.319 |
| Multiple locations | 2 (2.7) | 9 (15.8) | 0.011 |
| Abscess in TEE | 8 (11) | 8 (14) | 0.603 |
| Type of surgery | | | 0.039 |
| Elective | 47 (64) | 26 (46) | 0.035 |
| Urgent | 20 (27) | 28 (49) | 0.017 |
| Emergent | 6 (9) | 3 (5) | 0.731 |
| Symptom onset to diagnosis | 9(6, 21) | 15 (5, 30) | 0.884 |
| (days) | | | |
| The interval from diagnosis to | 14 (0, 42) | 14 (1, 56) | 0.834 |
| surgery (days) | | | |
| Referral source | 54 | 41 | 0.844 |
| Internal (In-house) | 19 (26) | 16 (28.1) | |
| External (Outside referring | 54 (74) | 41 (71.9) | |
| clinic) | | | |
| RMI: Rody Mass Index I V FF: Left V | Ventricular Fiection Fraction | n COPD: Chronic Obstructiv | e Pulmonary l |

BMI: Body Mass Index, LV EF: Left Ventricular Ejection Fraction, COPD: Chronic Obstructive Pulmonary Disease, CCS: Canadian Cardiovascular Society, NYHA: New York Heart Association, IE: Infective Endocarditis, TEE: Transesophageal Echocardiography

4.2. Patient Characteristics: PVE

The pre-pandemic prosthetic valve endocarditis (PVE) cohort was older than the post-pandemic cohort ($61 \pm 12.9 \text{ vs. } 70 \pm 9.9 \text{ years}$, p = 0.019). Similar to the NVE group, the post-pandemic PVE cohort showed a higher prevalence of advanced NYHA functional class III (24% vs. 66%, p = 0.004), which corresponded with an increase in urgent surgeries (20% vs. 52%, p = 0.034).

While the time from symptom onset to diagnosis was longer in the post-pandemic cohort, this was not statistically significant (7 days vs. 12 days, p = 0.330) (Figure 2). However, the interval from diagnosis to surgery was significantly prolonged in the post-pandemic cohort (11 days vs. 16 days, p = 0.038). Other comorbidities showed no significant differences and are detailed in Table 2.

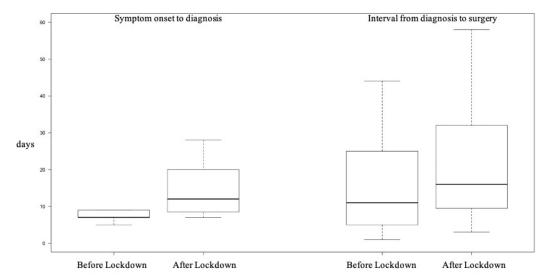


Figure 3: Time intervals from symptom onset to diagnosis and diagnosis to surgery in the PVE Cohort.

Table 2: Demographic and preoperative clinical characteristics of the PVE cohort (N=48).

| | 8/18 - 3/21/20 Before Lockdown Nr./Mean (%) | 3/22/20 - 11/21 After Lockdown Nr./Mean (%) | p-value |
|--------------------------------|---|---|---------|
| Cohort | 21 | 27 | |
| Age | 61 ± 12.9 | 70 ± 9.9 | 0.019 |
| Male | 11 (52) | 21 (78) | 0.423 |
| BMI | 25.1 ± 5.1 | 27.1 ± 6.3 | 0.331 |
| Creatinine mg/dl | 1.5 ± 1.1 | 1.4 ± 0.8 | 0.900 |
| Sinus rhythm | 20 (95) | 18 (67) | 0.029 |
| LV EF < 50% | 5 (24) | 2 (8) | 0.215 |
| COPD | 3 (14) | 3 (11) | 1.000 |
| Arterial Hypertension | 7 (33) | 13 (48) | 0.382 |
| Diabetes mellitus | 7 (33) | 13 (40) | 0.344 |
| No therapy | 1 (5) | 1 (4) | 1.000 |
| Oral medication | 0 | 3 (11) | 0.246 |
| Insulin therapy | 1 (5) | 3 (11) | 0.621 |
| Hyperlipidemia | 4 (20) | 5 (11) | 1.000 |
| Nicotine abuse | | | 0.683 |
| Alcohol abuse | 2 (10) 0 | 4 (15) | 1.000 |
| | | 1 (4) | |
| Family disposition | 2 (10) | 2 (8) | 1.000 |
| Coronary Artery Disease | 3 (14) | 14 (52) | 0.005 |
| CCS | 20 (05 2) | 25 (02 () | 0.651 |
| I | 20 (95.2) | 25 (92.6) | 1.000 |
| II | 1 (4.8) | 1 (3.7) | 1.000 |
| III | 0 | 0 | 1 000 |
| IV | 0 | 1 (3.7) | 1.000 |
| NYHA | | | 0.019 |
| I | 5 (24) | 1 (4) | 0.073 |
| II | 10 (47) | 7 (26) | 0.140 |
| III | 5 (24) | 18 (66) | 0.004 |
| IV | 1 (5) | 1 (4) | 1.000 |
| Rankin | | | 0.442 |
| No significant disability | 3 (14) | 2 (7) | 0.641 |
| Slight disability | 0 | 1 (4) | 1.000 |
| Moderate disability | 1 (5) | 0 | 0.438 |
| Modified Duke | | | 0.160 |
| Definite | 11 (53) | 20 (74) | 0.140 |
| Possible | 7 (33) | 3 (11) | 0.081 |
| rejected | 3 (14) | 4 (15) | 1.000 |
| IE valve position | | | |
| Aortic valve | 17 (81) | 16 (59.3) | 0.129 |
| Mitral valve | 4 (19) | 7 (25.9) | 0.733 |
| Tricuspid valve | 0 | 0 | |
| Multiple locations | 0 | 4 (14.8) | 0.121 |
| Abscess in TEE | 6 (40) | 9 (60) | 0.764 |
| Type of surgery | , , | , | 0.065 |
| Elective | 16 (76) | 12 (44) | 0.040 |
| Urgent | 4 (20) | 14 (52) | 0.034 |
| Emergent | 1 (4) | 1 (4) | 1.000 |
| Symptom onset to diagnosis | 7 (5, 9) | 12 (7, 28) | 0.330 |
| (days) | , (5, 7) | 12 (1, 20) | 0.550 |
| The interval from diagnosis to | 11 (1, 44) | 16 (3, 58) | 0.038 |
| surgery (days) | (-, 11) | 10 (0,00) | 0.050 |
| Referral source | | | 0.750 |
| Internal (In-house) | 7 (33.3) | 7 (25.9) | 0.750 |
| External (Outside referring | 14 (66.7) | 20 (74.1) | |
| clinic) | 11 (00.1) | 20 (/) | |

BMI: Body Mass Index, LV EF: Left Ventricular Ejection Fraction, COPD: Chronic Obstructive Pulmonary Disease, CCS: Canadian Cardiovascular Society, NYHA: New York Heart Association, IE: Infective Endocarditis, TEE: Transesophageal Echocardiography

4.3. Type of Cardiac Surgery

A significant decline in the number of IE surgeries was observed in both cohorts after the pandemic. The post-pandemic PVE cohort showed an increase in double-valve procedures compared to the pre-pandemic cohort (9.5% vs. 37%, p = 0.022). Cross-clamp times were not significantly different across groups (NVE pre-pandemic vs. post-pandemic: 87.0 ± 33.5 vs. 94.0 ± 44.6 minutes, p = 0.486; PVE pre-pandemic vs. post-pandemic: 105.8 ± 48.5 vs. 121.3 ± 50.7 minutes, p = 0.208) (Table 3 and 4).

Table 3: Types of surgical procedures performed in the NVE cohort.

| | Before Lockdown Nr. (%) | After Lockdown Nr. (%) | p-value |
|------------------------|-------------------------|------------------------|---------|
| Cross-clamp Time (min) | 87.0 ± 33.5 | 94 ± 44.6 | 0.486 |
| Single-valve procedure | | | |
| Isolated AV | 37 (50.7) | 19 (33.3) | 0.052 |
| Isolated MV | 24 (32.9) | 19 (33.3) | 1.000 |
| Isolated TV | 1(1.3) | 3 (5.3) | 0.319 |
| Double-valve procedure | 11 (15.1) | 14 (26.4) | 0.186 |
| Triple-valve procedure | 0 | 2 (3.7) | 0.190 |
| Total | 73 | 57 | |
| Concomitant CABG | 15 (20.5) | 19 (33.3) | 0.112 |
| ECMO use | 2 (2.7) | 1 (1.8) | 1.000 |

AV: Aortic Valve, MV: Mitral Valve, TV: Tricuspid Valve, CABG: Coronary Artery Bypass Grafting, ECMO: Extracorporeal Membrane Oxygenation

Table 4: Types of surgical procedures performed in the PVE cohort.

| | Before Lockdown Nr. (%) | After Lockdown Nr. (%) | p-value |
|------------------------|-------------------------|------------------------|---------|
| Cross-clamp Time (min) | 105.8 ± 48.5 | 121.3 ± 50.7 | 0.208 |
| Single-valve procedure | | | |
| Isolated AV | 13 (61.9) | 10 (37.0) | 0.244 |
| Isolated MV | 6 (28.6) | 5 (18.5) | 0.319 |
| Isolated TV | 0 | 2 (7.5) | |
| Double-valve procedure | 2 (9.5) | 10 (37.0) | 0.022 |
| Triple-valve procedure | 0 | 2 (7.5) | 1.000 |
| Total | 21 | 27 | |
| Concomitant CABG | 2 (9.5) | 6 (22.2) | 0.437 |
| ECMO use | 0 | 2 (7.5) | 0.497 |

AV: Aortic Valve, MV: Mitral Valve, TV: Tricuspid Valve, CABG: Coronary Artery Bypass Grafting, ECMO: Extracorporeal Membrane Oxygenation

4.4. Spectrum of Pathogens in Preoperative Blood Cultures

Across all cohorts, the most commonly identified pathogens were Staphylococci and Streptococci species, followed by Enterococcus faecalis. Detailed pathogen distributions are presented in Tables 4 and 5.

Table 5: Pathogen identified in the NVE cohort. Distribution of pathogens from preoperative blood cultures, focusing on Staphylococci, Streptococci, Enterococcus faecalis, and other less common pathogens, including Abiotrophia defective, Actinomyces naeslundii, Aggregatibacter aphrophilus, Bartonella quintana, Gemella morbillorum, Granulicatella advances, Neisseria elongate, Propionibacterium acnes.

| | Before Lockdown Nr. (%) | After Lockdown Nr. (%) | p value |
|-----------------------|-------------------------|------------------------|---------|
| Group of Germ | | | 0.220 |
| Staphylococci Group | 23 (31.5) | 17 (29.8) | |
| Streptococci Group | 20 (27.4) | 20 (35.1) | |
| Enterococcus faecalis | 5 (6.8) | 9 (15.8) | |
| ETC | 6 (8.2) | 2 (3.5) | |
| No germs | 19 (26) | 9 (15.8) | |
| Total | 73 | 57 | |

Table 6: Pathogens Identified in the PVE Cohort.

| | Before Lockdown Nr. (%) | After Lockdown Nr. (%) | p-value |
|-----------------------|-------------------------|------------------------|---------|
| Group of Germ | | | 0.574 |
| Staphylococci Group | 5 (23.8) | 8 (29.6) | |
| Streptococci Group | 4 (19) | 8 (29.6) | |
| Enterococcus faecalis | 1 (4.8) | 3 (11.1) | |
| ETC | 2 (9.5) | 1 (3.7) | |
| No germs | 9 (42.9) | 7 (25.9) | |
| Total | 21 | 27 | |

4.3. Surgical Outcomes

No significant differences in in-hospital mortality were observed across cohorts (NVE: p = 0.388; PVE: p = 0.152). However, the post-pandemic NVE cohort showed a significantly higher rate of re-thoracotomy due to postoperative bleeding (OR: 9.106 [2.502–33.144], p < 0.001).

For the post-pandemic PVE cohort, all postoperative outcomes showed an increased odds ratio (OR): inhospital mortality (4.000), stroke (1.000), re-thoracotomy (1.364), sepsis (1.120), delirium (1.188), hemofiltration (3.400), and tracheotomy (1.600). This resulted in a longer intensive care unit (ICU) stay (median 4.3 days vs. 8.1 days), although this was not statistically significant (p = 0.182). Detailed results are available in Tables 6 and 7, and Figures 3 and 4.

Table 7: Postoperative outcomes in the NVE cohort. ICU: Intensive Care Unit

| | Before/ Lockdown Nr. (%) | After Lockdown Nr. (%) | p-value |
|---------------------------|--------------------------|------------------------|---------|
| In-hospital mortality | 13 (17.8) | 14 (24.6) | 0.388 |
| Stroke | 7 (9.6) | 3 (5.3) | 0.512 |
| Rethoracotomy | 3 (4.1) | 16 (28.1) | < 0.001 |
| Infection or sepsis | 14 (19.2) | 7 (12.3) | 0.343 |
| Delirium | 8 (11.0) | 6 (10.5) | 1.000 |
| Hemofiltration | 13 (17.8) | 17 (29.8) | 0.142 |
| Tracheostomy | 1 (1.4) | 3 (5.3) | 0.319 |
| Length of ICU stay (days) | 5.4 ± 8.8 | 5.4 ± 13.2 | 0.991 |

ICU: Intensive Care Unit

Table 8: Postoperative Outcomes in the PVE cohort.

| | Before/ Lockdown Nr. (%) | After Lockdown Nr. (%) | p-value |
|---------------------------|--------------------------|------------------------|---------|
| In-hospital mortality | 2 (9.5) | 8 (29.6) | 0.152 |
| Stroke | 1 (4.8) | 2 (7.4) | 1.000 |
| Rethoracotomy | 3 (14.3) | 5 (18.5) | 1.000 |
| Infection or sepsis | 5 (23.8) | 7 (25.9) | 1.000 |
| Delirium | 2 (9.5) | 3 (11.1) | 1.000 |
| Hemofiltration | 4 (19.0) | 12 (44.4) | 0.075 |
| Tracheostomy | 1 (4.8) | 2 (7.4) | 1.000 |
| Length of ICU stay (days) | 4.3 ± 7.4 | 8.1 ± 10.9 | 0.182 |

ICU: Intensive Care Unit

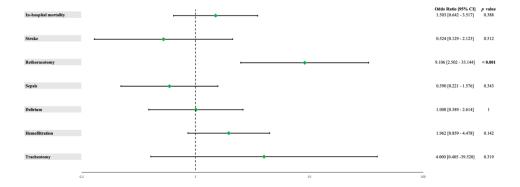


Figure 4: Forest plot of postoperative outcomes in the NVE Cohort. Odds ratios and confidence intervals for postoperative complications in the NVE cohort, contrasting pre- and post-pandemic periods.

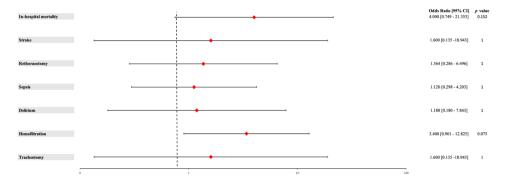


Figure 5: Forest Plot of Postoperative Outcomes in the PVE Cohort. A visual summary of postoperative complication odds in the PVE cohort, highlighting pandemic-related impacts.

5. Discussion

The COVID-19 pandemic significantly disrupted healthcare systems worldwide, including the management of patients with infective endocarditis (IE). Diagnostic efforts during the pandemic were heavily focused on COVID-19, often at the expense of other critical conditions. Triage protocols for intensive care unit (ICU) resources and ventilator availability further impacted surgical departments, delaying necessary interventions. Despite the publication of IE diagnostic guidelines during the pandemic, our findings align with global reports showing worse outcomes for IE patients during this period (Habib et al., 2008; Ivanovic et al., 2019; Ivert et al., 1984; J. S. Lee et al., 2024). However, as this study is limited to a single institution, caution is warranted in extrapolating our findings to other regions or healthcare systems.

Both NVE and PVE cohorts demonstrated more severe preoperative symptoms during the pandemic, necessitating a higher proportion of urgent surgeries (Table 1.1 and 1.2). PVE patients often presented with nonspecific symptoms, contrasting with the characteristic signs of NVE, such as fever, Janeway lesions, and Osler's nodes. Diagnostic challenges in PVE were further complicated by prosthesis-related artifacts in transthoracic echocardiography, requiring transesophageal echocardiography for improved sensitivity (Habib et al., 2008; Ivert et al., 1984). Patients with prosthetic valves were routinely issued implant cards and educated to present these cards during hospital visits to facilitate a more focused diagnostic approach to prosthetic valve endocarditis. Although this practice was intended to improve diagnostic efficiency by alerting physicians to the possibility of prosthetic valve infection, the observed time interval from symptom onset to diagnosis during the pandemic did not reflect a meaningful reduction, suggesting that other systemic factors influenced delays.

The interval from diagnosis to surgery was significantly prolonged in the PVE cohort, likely reflecting pandemic-driven restrictions. Daily institutional meetings to prioritize surgeries based on COVID-19 incidence rates and ICU bed availability further constrained timely interventions. The PVE cohort, comprising older patients with worsening symptoms, exhibited prolonged ICU stays, underscoring the complex perioperative challenges faced during the pandemic (J.-S. Lee et al., 2024).

Pathogen profiles in both cohorts were consistent across periods, with Staphylococci and Streptococci predominating. Advanced diagnostic techniques like FISHseq/PCR, which align with ISVC guidelines, enhanced pathogen detection (Eichinger et al., 2019). Notably, no nosocomial PVE cases were identified, suggesting that stringent hygiene protocols and restricted visitor policies during the pandemic mitigated hospital-acquired infections (Huang et al., 2021; Talic et al., 2021).

Postoperative outcomes revealed non-significant differences in in-hospital mortality. However, the NVE cohort experienced an increase in re-thoracotomies for bleeding, possibly due to higher preoperative risk profiles and systemic constraints during the pandemic. Elevated odds ratios for complications in the PVE cohort highlight the intensified perioperative challenges, with prolonged ICU stays further emphasizing the strain on resources. Although long-term outcomes were not the focus of this study, it is important to consider the potential lasting effects of pandemic-related surgical delays, including recurrent infections, valve dysfunction, and overall patient survival. Future research should explore these aspects through extended follow-up studies.

This study underscores the pandemic's cascading effects, from delayed diagnoses to increased surgical complexity and heightened postoperative morbidity. These findings emphasize the critical need for adaptable healthcare strategies to safeguard the management of non-COVID-19 conditions during public health crises. Consolidating global guidelines and lessons learned can help optimize IE management in future pandemics. Additionally, healthcare systems should develop strategies to mitigate selection bias and maintain continuity of care in emergencies, ensuring that high-risk patient populations receive timely interventions despite systemic disruptions.

6. Limitation

This retrospective subanalysis, conducted in a single-center setting, has inherent limitations. The small cohort size, particularly in the PVE group, restricts the generalizability of our findings to broader populations or healthcare

systems. Additionally, variability in data collection and patient selection introduces potential biases. The retrospective nature of the study also limits the ability to infer causality. Future multicenter studies with larger patient cohorts and longer-term follow-up data are essential to validate these findings and offer a more comprehensive understanding of the pandemic's impact on IE care. Further investigations should assess how pandemic-related delays influenced long-term outcomes, including valve durability, reoperation rates, and overall survival.

7. Conclusion

The COVID-19 pandemic had a profound impact on the management and outcomes of native and prosthetic valve endocarditis. Pandemic-related triage and resource allocation led to delayed diagnoses, worsening cardiac symptoms, and an increased need for urgent surgeries, particularly in the PVE cohort. Despite these challenges, overall mortality remained unchanged, reflecting the resilience and adaptability of surgical teams.

However, the increased postoperative complications in post-pandemic cohorts highlight the necessity for enhanced perioperative management strategies during systemic disruptions. Acknowledging the limitations of our study, including its single-center design and lack of long-term follow-up, future research should focus on evaluating the enduring effects of pandemic-related delays on patient outcomes. Lessons learned from the pandemic should inform the development of adaptive healthcare protocols to ensure continuity of care for IE patients in future public health emergencies. Healthcare policymakers must also consider implementing contingency plans that preserve access to critical surgical interventions while managing resource constraints during future crises.

Acknowledgement Statement: The authors would like to thank all participants, medical staff, and research collaborators for their valuable contributions to this study. We also extend our gratitude to the reviewers for their insightful comments and suggestions, which helped improve the quality of this manuscript.

Conflicts of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT Author contribution statements: [V.L.S.] conceptualized the study, contributed critical revisions, and supervised the research process. [A.M.] provided methodology. [W.E.] contributed to data interpretation and manuscript drafting. All co-authors provided critical revisions and supervised the research process. All authors reviewed and

approved the final manuscript.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement: Data is available at request. Please contact the corresponding author for any additional information on data access or usage.

Disclaimer: The views and opinions expressed in this article are those of the author(s) and contributor(s) and do not necessarily reflect JHVD's or editors' official policy or position. All liability for harm done to individuals or property as a result of any ideas, methods, instructions, or products mentioned in the content is expressly disclaimed.

References

- Ad, N., Luc, J. G. Y., Nguyen, T. C., & Group, C.-N. A. C. S. S. W. (2021). Cardiac surgery in North America and coronavirus disease 2019 (COVID-19): Regional variability in burden and impact. *J Thorac Cardiovasc Surg*, 162(3), 893-903 e894. https://doi.org/10.1016/j.jtcvs.2020.06.077
- Baddour, L. M., Wilson, W. R., Bayer, A. S., Fowler, V. G., Jr., Tleyjeh, I. M., Rybak, M. J., Barsic, B., Lockhart, P. B., Gewitz, M. H., Levison, M. E., Bolger, A. F., Steckelberg, J. M., Baltimore, R. S., Fink, A. M., O'Gara, P., Taubert, K. A., American Heart Association Committee on Rheumatic Fever, E., Kawasaki Disease of the Council on Cardiovascular Disease in the Young, C. o. C. C. O. C. S., Anesthesia, & Stroke, C. (2015). Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications: A Scientific Statement for Healthcare Professionals From the American Heart Association. Circulation, 132(15), 1435-1486. https://doi.org/10.1161/CIR.000000000000000296
- Delahaye, F., Alla, F., Beguinot, I., Bruneval, P., Doco-Lecompte, T., Lacassin, F., Selton-Suty, C., Vandenesch, F., Vernet, V., Hoen, B., & Group, A. (2007). In-hospital mortality of infective endocarditis: prognostic factors and evolution over 8 years. *Scand J Infect Dis*, 39(10), 849-857. https://doi.org/10.1080/00365540701393088
- Delgado, V., Ajmone Marsan, N., de Waha, S., Bonaros, N., Brida, M., Burri, H., Caselli, S., Doenst, T., Ederhy, S., Erba, P. A., Foldager, D., Fosbol, E. L., Kovac, J., Mestres, C. A., Miller, O. I., Miro, J. M., Pazdernik, M., Pizzi, M. N., Quintana, E., . . . Group, E. S. C. S. D. (2023). 2023 ESC Guidelines for the management of endocarditis. *Eur Heart J*, 44(39), 3948-4042. https://doi.org/10.1093/eurheartj/ehad193
- Eichinger, S., Kikhney, J., Moter, A., Wiessner, A., & Eichinger, W. B. (2019). Fluorescence in situ hybridization for identification and visualization of microorganisms in infected heart valve tissue in addition to standard diagnostic tests improves diagnosis of endocarditis. *Interact Cardiovasc Thorac Surg*, 29(5), 678-684. https://doi.org/10.1093/icvts/ivz159

- Habib, G., Thuny, F., & Avierinos, J. F. (2008). Prosthetic valve endocarditis: current approach and therapeutic options. *Prog Cardiovasc Dis*, 50(4), 274-281. https://doi.org/10.1016/j.pcad.2007.10.007
- Huang, F., Armando, M., Dufau, S., Florea, O., Brouqui, P., & Boudjema, S. (2021). COVID-19 outbreak and healthcare worker behavioural change toward hand hygiene practices. *J Hosp Infect*, 111, 27-34. https://doi.org/10.1016/j.jhin.2021.03.004
- Hunger, R., Konig, V., Stillger, R., & Mantke, R. (2022). Impact of the COVID-19 pandemic on delays in surgical procedures in Germany: a multi-center analysis of an administrative registry of 176,783 patients. *Patient Saf Surg*, 16(1), 22. https://doi.org/10.1186/s13037-022-00331-y
- Ivanovic, B., Trifunovic, D., Matic, S., Petrovic, J., Sacic, D., & Tadic, M. (2019). Prosthetic valve endocarditis A trouble or a challenge? *J Cardiol*, 73(2), 126-133. https://doi.org/10.1016/j.jjcc.2018.08.007
- Ivert, T. S., Dismukes, W. E., Cobbs, C. G., Blackstone, E. H., Kirklin, J. W., & Bergdahl, L. A. (1984). Prosthetic valve endocarditis. *Circulation*, 69(2), 223-232. https://doi.org/10.1161/01.cir.69.2.223
- Lalani, T., Chu, V. H., Park, L. P., Cecchi, E., Corey, G. R., Durante-Mangoni, E., Fowler, V. G., Jr., Gordon, D., Grossi, P., Hannan, M., Hoen, B., Munoz, P., Rizk, H., Kanj, S. S., Selton-Suty, C., Sexton, D. J., Spelman, D., Ravasio, V., Tripodi, M. F., . . . International Collaboration on Endocarditis-Prospective Cohort Study, I. (2013). In-hospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis. JAMA Intern Med, 173(16), 1495-1504. https://doi.org/10.1001/jamainternmed.2013.8203
- Lee, J.-S., Sales, V. L., Schwaiger, B., Eszlari, E., Lieber, M., Hohe, S., & Eichinger, W. (2024). Impact of COVID-19 lockdown on adult cardiac surgery and patient outcomes in a German tertiary care center. *Journal of Public Health*. https://doi.org/10.1007/s10389-024-02381-1
- Lee, J. S., Sales, V. L., Moter, A., & Eichinger, W. (2024). Early Surgical Outcomes in Infective Endocarditis Before and During COVID-19 Pandemic. *Thorac Cardiovasc Surg.* https://doi.org/10.1055/a-2489-6268
- Talic, S., Shah, S., Wild, H., Gasevic, D., Maharaj, A., Ademi, Z., Li, X., Xu, W., Mesa-Eguiagaray, I., Rostron, J., Theodoratou, E., Zhang, X., Motee, A., Liew, D., & Ilic, D. (2021). Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis. *Bmj*, 375, e068302. https://doi.org/10.1136/bmj-2021-068302