Recent Surgical Results for Active Endocarditis Complicated With Perivalvular Abscess

Daisuke Yoshioka, MD; Koichi Toda, MD; Jun-ya Yokoyama, MD; Ryohei Matsuura, MD; Shigeru Miyagawa, MD; Yukitoshi Shirakawa, MD; Toshiki Takahashi, MD; Taichi Sakaguchi, MD; Hirotugu Fukuda, MD; Yoshiki Sawa, MD

Background: Surgical treatment for endocarditis patients with a perivalvular abscess is still challenging.

Methods and Results: From 2009 to 2016, 470 patients underwent surgery for active endocarditis at 11 hospitals. Of these, 226 patients underwent aortic valve surgery. We compared the clinical results of 162 patients without a perivalvular abscess, 37 patients who required patch reconstruction of the aortic annulus (PR group) and 27 who underwent aortic root replacement (ARR group).

Patients with a perivalvular abscess had a greater number of Staphylococcus species and prosthetic valve endocarditis, a greater level of inflammation at diagnosis and symptomatic heart failure before surgery, especially in the ARR group. Nevertheless, the duration between diagnosis and surgery was similar, because of a high prevalence of intracranial hemorrhage in the ARR group.

Hospital death occurred in 13 (9%) patients without a perivalvular abscess, in 4 (12%) in the PR and in 7 (32%) in the ARR group. Postoperative inflammation and end-organ function were similar between the groups. Overall survival of patients without a perivalvular abscess and that of the PR group was similar, but was significantly worse in the ARR group (P=0.050, 0.026). Freedom from endocarditis recurrence was similar among all patients.

Conclusions: Patients treated with patch reconstruction showed favorable clinical results. Early surgical intervention is necessary when a refractory invasive infection is suspected.

Key Words: End-organ function; Endocarditis; Perivalvular abscess

Acute infective endocarditis (IE) is a life-threatening disease characterized by high rates of morbidity and death. Peri-annular complications occur in approximately 9.8–40% of affected patients and surgery is a challenge, particularly in cases of complete aortic root destruction. Aortic root abscesses that remain confined with minimal or no destruction of surrounding tissues are usually successfully managed by radical excision of all infected tissues, followed by pericardial patch reconstruction and aortic valve replacement (AVR), but a large abscess that has destroyed the entire aortic annulus and extends proximally into the left ventricular outflow tract often requires complex aortic root replacement (ARR). However, few reports have investigated the results of surgery for endocarditis in patients with a perivalvular abscess as compared with those without. Thus, in the present study we evaluated the clinical results of patients with a perivalvular abscess who underwent complex surgery for aortic valve endocarditis.

Methods

Patients

This retrospective multicenter study was approved by the Review Board of Osaka University Hospital and use of the Osaka Cardiovascular Research Group (OSCAR) database was approved by each affiliated hospital. Detailed records of patients who underwent valve surgery for active left-side endocarditis since 2009 at 11 affiliated hospitals were obtained.

From 2009 to 2016, 470 patients underwent valve surgery for left-side active endocarditis at the 11 hospitals (Figure S1, Appendix S1). Of those, 226 had active endocarditis involving the aortic valve. They were divided into patients who required only AVR or a vegetectomy (without perivalvular abscess, n=162), and those who required complex valve surgery for aortic annulus involvement (with perivalvular abscess, n=64). The latter 64 with a perivalvular abscess were further divided into patients who required AVR with
vegetation was confirmed by transthoracic or transesophageal echocardiography. In cases without confirmation of vegetation, the timing of diagnosis was the day when Duke’s criteria were met. Active endocarditis was defined as endocarditis requiring antibiotic therapy until surgery; cases of healed endocarditis were excluded. Perivalvular abscess was confirmed by operative record and defined as a case of endocarditis that required a surgical procedure to reconstruct a defective annulus after complete debridement of

| Table 1. Characteristics of Study Patients at Time of Endocarditis Diagnosis | Perivalvular abscess (−) (n=162) | Perivalvular abscess (+) (n=64) | P value | PR group (n=37) | ARR group (n=27) | P value |
|---|---|---|---|---|---|---|
| Baseline characteristics | | | | | | |
| Age (years) | 62.2±14.9 | 64.8±14.4 | 0.243 | 66.1±14.5 | 63.1±14.5 | 0.410 |
| Male, n (%) | 112 (69) | 42 (66) | 0.636 | 25 (68) | 17 (63) | 0.792 |
| Body surface area (m²) | 1.56±0.19 | 1.56±0.21 | 0.919 | 1.57±0.14 | 1.54±0.29 | 0.708 |
| Body mass index (kg/m²) | 21.9±4.2 | 22.6±4.5 | 0.563 | 22.2±4.3 | 22.2±4.9 | 0.751 |
| Bacterial species | | | | | | |
| Positive blood culture, n (%) | 116 (72) | 51 (80) | 0.242 | 29 (78) | 22 (81) | 1.000 |
| *Staphylococcus* sp. | 40 (25) | 30 (47) | 0.002 | 19 (51) | 11 (41) | 0.423 |
| *Staphylococcus aureus*, n (%) | 21 (13) | 17 (26) | 0.018 | 7 (19) | 10 (37) | 0.152 |
| MRSA, n (%) | 10 (6) | 5 (8) | 0.767 | 3 (8) | 2 (7) | 1.000 |
| Streptococcus sp., n (%) | 63 (39) | 13 (20) | 0.008 | 8 (22) | 5 (19) | 1.000 |
| Comorbidities | | | | | | |
| Atrial fibrillation, n (%) | 15 (9) | 11 (17) | 0.107 | 6 (16) | 5 (19) | 1.000 |
| Hemodialysis, n (%) | 20 (12) | 6 (9) | 0.647 | 3 (8) | 3 (11) | 0.691 |
| Hypertension, n (%) | 54 (33) | 20 (31) | 0.875 | 14 (38) | 6 (22) | 0.275 |
| Diabetes mellitus, n (%) | 31 (19) | 18 (28) | 0.154 | 8 (21) | 10 (37) | 0.260 |
| Insulin use, n (%) | 13 (42) | 6 (42) | 0.762 | 3 (30) | 3 (30) | 1.000 |
| Antiplatelet therapy, n (%) | 24 (15) | 22 (34) | 0.002 | 14 (38) | 8 (30) | 0.598 |
| Anticoagulation therapy, n (%) | 12 (7) | 17 (27) | <0.001 | 11 (30) | 6 (22) | 0.576 |
| Affected valve | | | | | | |
| Mitral valve involvement, n (%) | 71 (44) | 14 (22) | 0.002 | 5 (14) | 9 (33) | 0.072 |
| Prosthetic aortic valve endocarditis, n (%) | 22 (14) | 36 (56) | <0.001 | 21 (57) | 15 (58) | 1.000 |
| Echocardiographic parameters | | | | | | |
| LVDd (mm) | 55.5±8.1 | 53.8±8.6 | 0.181 | 54.5±8.6 | 52.9±8.6 | 0.492 |
| LVDs (mm) | 36.1±8.2 | 35.2±8.5 | 0.501 | 35.2±8.4 | 35.3±8.9 | 0.997 |
| EF (%) | 62.5±11.5 | 63.8±10.1 | 0.437 | 64.6±10.4 | 62.8±9.9 | 0.531 |
| Systolic tricuspid pressure gradient (mmHg) | 37.0±16.1 | 35.0±14.8 | 0.513 | 37.4±15.8 | 30.5±11.8 | 0.175 |
| Maximum length of vegetation (mm) | 11.9±6.0 | 10.4±5.6 | 0.152 | 9.0±6.1 | 12.2±4.4 | 0.070 |
| Grade of aortic regurgitation | 2.7±1.3 | 2.4±1.4 | 0.059 | 2.6±1.2 | 2.0±1.5 | 0.106 |
| Laboratory data at diagnosis | | | | | | |
| WBC count (×1,000/μL) | 11.6±5.7 | 12.3±6.3 | 0.387 | 11.9±5.7 | 13.0±7.1 | 0.531 |
| C-reactive protein (mg/dL) | 6.8 (3.4–10.9) | 7.9 (4.3–14.2) | 0.047 | 7.6 (4.1–10.5) | 10.5 (5.8–20.7) | 0.131 |
| Hemoglobin (g/dL) | 10.2±2.2 | 10.5±1.8 | 0.453 | 10.1±1.5 | 11.0±2.1 | 0.057 |
| Platelet count (×1,000/μL) | 185±114 | 151±88 | 0.040 | 166±88 | 129±84 | 0.113 |
| Blood urea nitrogen (mg/dL) | 24.3±15.3 | 29.4±20.3 | 0.052 | 30.1±22.5 | 28.4±17.2 | 0.761 |
| Creatinine (mg/dL) | 0.92 (0.76–1.38) | 1.10 (0.79–1.72) | 0.354 | 1.08 (0.70–1.75) | 1.11 (0.81–1.69) | 0.645 |
| eGFR (mL/min/1.73m²) | 78.9±43.8 | 71.4±42.6 | 0.267 | 74.6±47.8 | 66.4±33.5 | 0.473 |
| Total bilirubin (mg/dL) | 0.7 (0.5–1.1) | 0.9 (0.6–1.3) | 0.137 | 0.8 (0.6–1.3) | 0.9 (0.6–1.3) | 0.722 |
| Lactate dehydrogenase (IU/L) | 297 (242–425) | 377 (295–467) | 0.032 | 380 (308–475) | 363 (261–464) | 0.775 |
| Total protein (mg/dL) | 6.38±0.85 | 6.31±0.81 | 0.625 | 6.50±0.83 | 6.08±0.74 | 0.062 |
| Albumin (mg/dL) | 2.90±0.58 | 2.79±0.50 | 0.250 | 2.78±0.49 | 2.75±0.48 | 0.846 |
| International normalization ratio | 1.45±0.95 | 1.49±0.54 | 0.796 | 1.57±0.65 | 1.38±0.36 | 0.225 |

ARR, aortic root replacement; EF, ejection fraction; eGFR, estimated glomerular filtration rate; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; MRSA, methicillin-resistant *Staphylococcus aureus*; PR, patch reconstruction of the annulus; WBC, white blood cell.

patch reconstruction of the aortic annulus (PR group, n=37) and those who required complete ARR because of severe destruction of the aortic annulus (ARR group, n=27). We analyzed and compared the preoperative characteristics and clinical results of these groups.

**Acute Endocarditis and Perivalvular Abscess**

All patients satisfied the Duke’s criteria. The timing of diagnosis of endocarditis was defined as the day when vegetation was confirmed by transthoracic or transesophageal echocardiography. In cases without confirmation of vegetation, the timing of diagnosis was the day when Duke’s criteria were met. Active endocarditis was defined as endocarditis requiring antibiotic therapy until surgery; cases of healed endocarditis were excluded. Perivalvular abscess was confirmed by operative record and defined as a case of endocarditis that required a surgical procedure to reconstruct a defective annulus after complete debridement of...
the abscess or complete replacement of the aortic root during valve surgery because of the severe destruction. Cases of very limited perivalvular abscess that did not require reconstruction of the annulus and treated by simple AVR were not considered to have a perivalvular abscess for the present analyses.

Valve Surgery
As this was a retrospective multicenter study, the timing of valve surgery was decided by the attending surgeon at each hospital. The main surgical strategy was complete debridement and excision of all infected tissue. The choice of valve prosthesis or conduit, whether mechanical or biological, was at the discretion of the attending surgeon. Ensuing defects in the aortic root were addressed either by ARR or reconstruction of the affected annulus with autologous or bovine pericardium, depending on the extent of aortic root involvement. For patients with an annulus and/or Valsalva sinus that was too severely invaded to reconstruct with a pericardial patch, ARR with a Bentall procedure or replacement with a Freestyle stentless valve (Medtronic®, Dublin, Ireland) or Prima Plus® stentless valve (Edwards Lifesciences, Irvine, CA, USA) was generally performed.

Data Collection, and Laboratory and Echocardiographic Data
Collection of data regarding the present patients was organized by 3 surgeons (D.Y., J.Y., R.M.). Patient identification was done using the OSCAR database and details were collected from hospital medical records. Echocardiographic parameters were obtained at the time of diagnosis of endocarditis. Vegetation size was based on maximal length measured during echocardiography performed at the time of diagnosis. Laboratory data were obtained from medical records at the time of endocarditis diagnosis, just before valve surgery, and at 1, 2, 4, and 8 weeks after surgery. Estimated glomerular filtration rate (eGFR) was calculated using the following equation: $186 \times (serum\ creatinine/88.4) - 1.154 \times (age\ in\ years)^{0.203} \times (serum\ calcium/88.4)$ −1.154 (for female). Acute preoperative cerebral infarction was defined as the presence of an acute infarct lesion in the brain shown by computed tomography (CT) or magnetic resonance imaging. Preoperative acute intracranial hemorrhage was defined as the presence of a high-density hemorrhagic lesion in the brain on CT. Other embolisms were defined as the presence of any infarct lesion shown by systemic CT scanning or clinical symptoms of an embolism in the extremities (e.g., Osler node). As for postoperative complications, neurological deterioration was defined as persistent worsening of a neurological symptom as compared with preoperative condition. Transient neurological symptoms without any evidence of a new lesion on neuroimaging were not considered to be neurological deterioration. Complete atrioventricular (AV) block was defined as requiring pacemaker implantation.

Follow-up investigations were performed using information obtained from medical records or from telephone contact by a physician. The mid-term follow-up data were also collected in this study. Mid-term death was defined as any-cause death. Cardiovascular-related death was defined as death from cardiovascular disease, which included stroke, heart failure, sudden death, prosthetic valve endocarditis,

---

### Table 2. Characteristics of Study Group of IE Patients Before Surgery

| Time after diagnosis (days) | Perivalvular abscess (−) (n=162) | Perivalvular abscess (+) (n=64) | P value | PR group (n=37) | ARR group (n=27) | P value |
|----------------------------|----------------------------------|---------------------------------|---------|----------------|----------------|---------|
| Complications              |                                   |                                 |         |                |                |         |
| Acute cerebral infarction, n (%) | 54 (33)                          | 23 (37)                         | 0.756   | 12 (32)        | 11 (41)        | 0.601   |
| Acute intracranial hemorrhage, n (%) | 9 (6)                            | 10 (16)                         | 0.030   | 2 (5)          | 8 (30)         | 0.013   |
| Systemic embolics, n (%)   | 68 (42)                          | 26 (42)                         | 1.000   | 13 (35)        | 13 (52)        | 0.203   |
| Hemodynamic status         |                                  |                                 |         |                |                |         |
| Symptomatic HF, n (%)      | 89 (55)                          | 43 (67)                         | 0.101   | 25 (68)        | 18 (67)        | 1.000   |
| Inotropes, n (%)           | 42 (26)                          | 23 (36)                         | 0.145   | 11 (30)        | 12 (44)        | 0.294   |
| Intubated, n (%)           | 23 (14)                          | 11 (17)                         | 0.544   | 2 (5)          | 9 (33)         | 0.006   |
| Surgical indication        |                                  |                                 |         |                |                |         |
| Refractory HF, n (%)       | 57 (36)                          | 29 (45)                         | 0.173   | 16 (43)        | 13 (48)        | 0.801   |
| Refractory infection, n (%)| 33 (20)                          | 22 (34)                         | 0.038   | 13 (35)        | 9 (33)         | 1.000   |
| High risk of embolism, n (%) | 48 (30)                         | 18 (28)                         | 0.872   | 9 (24)         | 9 (33)         | 0.575   |
| Laboratory data before surgery |                                |                                 |         |                |                |         |
| WBC count (×1,000/μL)      | 9.3±5.1                          | 11.2±6.2                        | 0.023   | 10.5±5.6       | 12.2±7.0       | 0.308   |
| C-reactive protein (mg/dL) | 3.4 (1.1–7.9)                    | 5.6 (2.9–9.3)                   | 0.004   | 5.1 (2.7–9.1)  | 6.5 (3.4–10.5) | 0.615   |
| Hemoglobin (g/dL)          | 10.3±2.0                         | 10.0±1.8                        | 0.277   | 9.8±1.7        | 10.2±1.9       | 0.323   |
| Platelet count (×1,000/μL) | 179±88                           | 167±87                          | 0.361   | 177±81         | 151±95         | 0.246   |
| Blood urea nitrogen (mg/dL)| 23.8±15.7                        | 28.3±19.1                       | 0.078   | 29.5±20.9      | 26.5±16.5      | 0.552   |
| Creatinine (mg/dL)         | 1.00 (0.74–1.37)                 | 1.01 (0.80–1.90)                | 0.467   | 1.27 (0.75–2.05)| 0.97 (0.75–1.70)| 0.464   |
| eGFR (mL/min/1.73m²)       | 77.8±42.8                        | 74.4±46.9                       | 0.606   | 71.7±46.8      | 78.3±47.6      | 0.588   |
| Total bilirubin (mg/dL)    | 0.6 (0.4–0.9)                    | 0.7 (0.4–1.1)                   | 0.316   | 0.7 (0.4–1.2)  | 0.8 (0.5–1.0)  | 0.868   |
| Lactate dehydrogenase (IU/L)| 297 (229–418)                    | 358 (256–457)                   | 0.102   | 322 (241–432)  | 421 (272–466)  | 0.472   |
| International normalization ratio | 1.28±0.39                        | 1.49±0.66                       | 0.006   | 1.55±0.76      | 1.41±0.49      | 0.441   |
and acute myocardial infarction. CVA (cerebrovascular accident)-related death was defined as any death caused by a major stroke. Infection-related death was defined as death from any infection (e.g., recurrence of endocarditis, pneumonia). Multiple organ failure (MOF)-related death was defined as any death caused by MOF, but did not include death from heart failure. Endocarditis recurrence was defined as IE that required redo valve surgery for definitive prosthetic valve endocarditis or definitive endocarditis that met Duke’s criteria and required prolonged intravenous antibiotic therapy.

### Statistical Analysis

Statistical analyses were performed using JMP version 11.0 (SAS Institute Inc., Cary, CA, USA). Categorical variables are presented as percentages, and continuous data as the mean, standard deviation, or median (interquartile range). Comparisons between 2 groups were performed using a chi-square test with categorical variables, t-test, or Wilcoxon test, as appropriate. All P-values for statistical analysis were two-tailed and P<0.05 indicated a statistically significant difference.

Overall survival and freedom from recurrence of endocarditis were estimated using Kaplan-Meier curves, and compared among the groups using a log-rank test.

### Results

Patient characteristics at the time of endocarditis diagnosis are summarized in Table 1. Those with a perivalvular abscess had a greater number of Staphylococcus species related to endocarditis and fewer Streptococcus species as compared with patients without a perivalvular abscess. There were no statistical differences in baseline characteristics, bacterial species, and comorbidities between the PR and ARR groups. Mitral valve involvement was significantly greater in patients without perivalvular abscess, probably because prosthetic valve endocarditis was more prevalent in the patients with a perivalvular abscess. In the overall 226 patients, the presence of mitral valve involvement was

### Table 3. Operative Results for Study Group of IE Patients

|                         | Perivalvular abscess (−) (n=162) | Perivalvular abscess (+) (n=64) | P value | PR group (n=37) | ARR group (n=27) | P value |
|-------------------------|----------------------------------|---------------------------------|---------|-----------------|-----------------|---------|
| **Aortic valve**        |                                  |                                 |         |                 |                 |         |
| Bioprosthetic valve, n (%) | 128 (79)                       | 59 (92)                        | 0.059   | 33 (89)         | 26 (96)         | 0.275   |
| Mechanical valve, n (%)   | 33 (20)                         | 5 (8)                          |         | 4 (11)          | 1 (4)           |         |
| Vegetectomy, n (%)      | 1 (1)                           | 0 (0)                          |         |                 |                 |         |
| **Concomitant mitral valve surgery** |                  |                                 |         |                 |                 |         |
| Valve replacement, n (%) | 45 (63)                         | 7 (50)                         | 0.380   | 2 (40)          | 5 (55)          | 1.000   |
| Bioprosthetic valve, n (%) | 33 (73)                        | 7 (100)                        | 0.314   | 2 (100)         | 5 (100)         | 1.000   |
| Mechanical valve, n (%) | 12 (27)                         | 0 (0)                          |         | 0 (0)           | 0 (0)           |         |
| **Operative times and transfusion** |                            |                                 |         |                 |                 |         |
| Operative time (min)      | 347±139                       | 530±217                        | <0.001  | 439±155         | 658±231         | <0.001  |
| CPB time (min)              | 187±84                      | 300±137                        | <0.001  | 250±93          | 368±159         | 0.001   |
| Aortic clamp time (min)    | 139±62                       | 208±85                         | <0.001  | 176±61          | 250±95          | 0.001   |
| Platelet transfusion (units) | 10 (0–20)                   | 20 (10–40)                    | 0.001   | 15 (0–20)       | 40 (25–50)      | 0.002   |
| **Complications**          |                                  |                                 |         |                 |                 |         |
| Neurological deterioration, n (%) | 12 (7)                     | 2 (3)                         | 0.360   | 1 (3)           | 1 (4)           | 1.000   |
| Mediastinitis, n (%)       | 1 (1)                          | 1 (2)                          | 0.487   | 1 (3)           | 0 (0)           | 1.000   |
| Requiring CVVHD, n (%)     | 23 (14)                        | 17 (26)                        | 0.034   | 7 (19)          | 10 (37)         | 0.152   |
| Complete AV block, n (%)   | 2 (1)                          | 7 (11)                         | 0.003   | 3 (8)           | 4 (15)          | 0.443   |
| Intubation duration (days) | 1 (1–3)                        | 2 (1–5)                        | 0.005   | 2 (1–5)         | 3 (1–6)         | 0.216   |
| Intravenous antibiotics duration (days) | 28 (21–41) | 34 (25–42)                    | 0.228   | 31 (20–42)      | 36 (28–40)      | 0.980   |
| Hospital stay (days)       | 39 (24–61)                     | 43 (31–55)                     | 0.548   | 45 (34–66)      | 40 (31–46)      | 0.264   |
| **Postoperative echocardiography** |                            |                                 |         |                 |                 |         |
| EF (%)                     | 56.9±14.1                     | 57.1±14.4                      | 0.953   | 56.4±12.6       | 57.4±15.5       | 0.827   |
| Perivalvular leakage, n (%) | 12 (7)                     | 5 (8)                         | 1.000   | 4 (11)          | 1 (4)           | 0.387   |
| **Mortality rates**        |                                  |                                 |         |                 |                 |         |
| 30-day, n (%)              | 8 (5)                          | 13 (19)                        | 0.079   | 3 (8)           | 5 (19)          | 0.266   |
| Hospital, n (%)            | 14 (9)                         | 17 (26)                        | 0.097   | 4 (11)          | 7 (26)          | 0.179   |
| **Cause of death (include duplication)** |               |                                 |         |                 |                 |         |
| HF, n (%)                  | 1 (1)                          | 4 (6)                          | 0.024   | 2 (5)           | 2 (7)           | 1.000   |
| Infection, n (%)           | 3 (2)                          | 5 (8)                          | 0.043   | 3 (8)           | 2 (7)           | 1.000   |
| CVA, n (%)                 | 4 (2)                          | 0 (0)                          | 0.579   | 0 (0)           | 0 (0)           | 1.000   |
| MOF, n (%)                 | 4 (2)                          | 6 (9)                          | 0.033   | 1 (3)           | 5 (19)          | 0.075   |

AV, atrioventricular; CPB, cardiopulmonary bypass; CVA, cerebrovascular accident; CVVHD, continuous veno-venous hemodialysis; EF, ejection fraction; MOF, multiple organ failure. Other abbreviations as in Tables 1,2.
Surgery for IE With Perivalvular Abscess

Citations for surgery, refractory infection was prevalent in patients with a perivalvular abscess. White blood cell count and serum CRP level were significantly higher in patients with a perivalvular abscess, but there were no differences in laboratory data between the PR and ARR groups.

Operative details are shown in Table 3. Of the 27 patients in the ARR group, 5 underwent ARR with a Freestyle stentless valve, 8 with a Prima Plus stentless valve, 6 with a Gelweave Valsalva® (Terumo, Japan) graft and bioprosthetic valve, 7 with a Hemashield® (MAQUET, Germany) graft and bioprosthetic valve, and 1 with a Hemashield graft and mechanical valve. Of the 37 patients in the PR group, nearly all required a bovine or autologous pericardial patch to reconstruct the defective annulus following sufficient debridement. The majority underwent valve replacement with a bioprosthetic valve regardless of the presence of a perivalvular abscess. Concomitant mitral valve surgery was performed in 71 (44%) patients without and in 14 (43%) in native valve endocarditis and 21% in prosthetic valve endocarditis (P=0.003). In 168 patients with native valve endocarditis, there was no statistical difference for mitral valve involvement between patients with and without perivalvular abscess. There was a trend of greater maximum vegetation length on echocardiography in the ARR group. Patients with a perivalvular abscess had higher levels of C-reactive protein (CRP) and lactate dehydrogenase, and lower platelet count.

Table 4. Changes in Pre- and Postoperative Laboratory Data for Study IE Patients

|                  | Preoperative          | Postoperative         |
|------------------|-----------------------|-----------------------|
|                  | Diagnosis Before operation | 1 week | 2 weeks | 4 weeks | 8 weeks |
| WBC count (x1,000/μL) | 11.6±5.7 | 9.3±5.1 | 9.0±4.0 | 7.7±3.1 | 6.1±2.2 | 6.5±2.4 |
| Perivalvular abscess (−) | 12.3±6.3 | 11.2±6.2* | 9.8±5.4 | 8.6±4.4 | 7.5±4.4* | 7.4±2.6 |
| C-reactive protein (mg/dL) | 6.8 (3.4–10.9) | 3.4 (1.1–7.9) | 4.9 (3.1–8.1) | 2.9 (1.2–4.9) | 0.8 (0.4–2.3) | 0.2 (0.1–1.1) |
| Perivalvular abscess (+) | 7.9 (4.3–14.2)* | 5.6 (2.9–9.3)* | 6.7 (4.2–9.5)* | 3.5 (1.7–7.7) | 1.4 (0.5–5.4)* | 0.9 (0.1–1.8) |
| eGFR (mL/min/1.73m²) | 78.9±43.8 | 77.8±42.8 | 80.5±43.0 | 79.8±45.5 | 81.0±41.8 | 75.1±37.5 |
| Perivalvular abscess (−) | 71.4±42.6 | 74.4±46.9 | 77.8±52.5 | 74.1±47.4 | 87.2±61.4 | 83.2±69.3 |
| Total bilirubin (mg/dL) | 0.7 (0.5–1.1) | 0.6 (0.4–0.9) | 0.9 (0.5–1.7) | 0.7 (0.4–1.0) | 0.6 (0.4–1.0) | 0.6 (0.4–0.8) |
| Perivalvular abscess (+) | 0.9 (0.6–1.3) | 0.7 (0.4–1.1) | 1.1 (0.6–2.5) | 0.8 (0.4–1.7) | 0.5 (0.4–0.7) | 0.5 (0.4–0.7) |
| Lactate dehydrogenase (IU/L) | 297 (242–425) | 297 (229–418) | 353 (287–450) | 346 (259–442) | 273 (225–373) | 265 (228–328) |
| Perivalvular abscess (+) | 377 (295–467)* | 358 (256–457) | 447 (320–609)* | 389 (292–545) | 335 (257–428) | 272 (235–345) |

*P<0.05 vs. patients without perivalvular abscess. Abbreviations as in Table 1.

Figure 1. (A) Overall survival and 95% confidence intervals for patients with (red) and without (blue) perivalvular abscess. (B) Overall survival for patients without perivalvular abscess (blue), and those who underwent patch reconstruction (PR group, purple) or aortic root replacement (ARR group, red).
Postoperative complications are also shown in Table 3. Patients with a perivalvular abscess more frequently required temporal continuous veno-venous hemodialysis (CVVHD) after surgery and had a more complete AV

(22%) with a perivalvular abscess (P=0.002). Operative, cardiopulmonary bypass, and aortic cross-clamping times were significantly longer in patients with a perivalvular abscess, especially in the ARR group.

Figure 2. (A) Overall survival after the first discharge for patients with (red) and without (blue) perivalvular abscess. (B) Overall survival after the first discharge for patients without perivalvular abscess (blue), and those who underwent patch reconstruction (PR group, purple) or aortic root replacement (ARR group, red).

Figure 3. Freedom from (A) major cardiovascular event-related death, (B) infection-related death, (C) cerebrovascular accident-related death, and (D) multiple organ failure-related death. (Blue: patients without perivalvular abscess; purple: patch reconstruction group; red: aortic root replacement group)
Surgery for IE With Perivalvular Abscess

The overall survival after the first discharge is shown in Figure 2. There was no statistical difference between patients with and without a perivalvular abscess. Overall survival after the first discharge was 76%, 69%, and 69% at 1, 3, and 5 years, respectively, in the ARR group.

We further analyzed the freedom from major cardiovascular events-related death, infection-related death, CVA-related death, and MOF-related death (Figure 3). In these analyses, there was a significant difference in major cardiovascular events-related death and MOF-related death among the groups; however, there was no statistical differences in infection-related and CVA-related deaths.

Freedom from endocarditis recurrence after 1, 3, and 5 years in patients without a perivalvular abscess was 97%, 93%, and 93%, respectively, and 98%, 90%, and 84%, respectively, in those with a perivalvular abscess (P=0.381) (Figure 4A). In total, 6 (4%) patients without a perivalvular abscess had a recurrence, of whom 2 underwent AVR only and the other 4 patients had a double valve replacement, including 1 with redo AVR for prosthetic valve endocarditis performed following the initial diagnosis of endocarditis.

A total of 4 (6%) patients with a perivalvular abscess developed endocarditis recurrence. For the initial surgery, 1 required a Bentall procedure with a Prima Plus stentless valve conduit and the other 3 underwent reconstruction of the aortic annulus with a pericardial patch. There was no statistical difference between the PR and ARR groups for freedom from endocarditis recurrence (Figure 4B).

Discussion

In the present study, (1) patients with a perivalvular abscess were in a more severe preoperative condition with a greater prevalence of prosthetic valve endocarditis and number of Staphylococcus species, higher level of inflammation, and low platelet count, trends that were more evident in the ARR group; (2) postoperative morbidity and mortality were higher in patients with a paravalvular abscess, but mainly occurred in the acute phase in the ARR group, whereas the clinical results for the PR group were comparable with those of patients without a perivalvular abscess.
and mid-term results after the first discharge was similar among the 3 groups; (3) the higher mortality rate in the ARR group was mainly related to major cardiovascular events-related or MOF-related death, because CVA-related and infection-related deaths were similar in number among the groups; and (4) there was a favorable level of endocarditis recurrence among the groups.

There are several reports on the clinical results of patients with endocarditis and a perivalvular abscess, but few have compared patients with and without a perivalvular abscess, or patients undergoing patch reconstruction and those having a full ARR. In those reports, the operative mortality rate for patients with a perivalvular abscess ranges from 15% to 20%, similar to the present findings. Leontyev et al recently reported no difference for 30-day death and long-term overall survival between patients who required patch reconstruction of the aortic annulus and those who required ARR, though the latter had a greater prevalence of prosthetic valve endocarditis, higher logistic Euro score, and longer cardiopulmonary bypass time. In the present study, though 30-day death for the ARR group was similar to the previous report, clinical results in the PR group were better. There was no statistical difference between patients without a perivalvular abscess and the PR group with regard to deaths (30-day, in-hospital, overall), postoperative complications (requirement for CVVHD, mediastinitis or complete AV block), or treatment duration (ventilation, intravenous antibiotics, hospital stay). Our results suggested that AVR with patch reconstruction for a defective annulus after complete debridement of infected tissue is an effective treatment with clinical results comparable to those of patients without a perivalvular abscess.

Obtaining good clinical results in the ARR group was challenging. These patients in the ARR group tended to have a high prevalence of *Staphylococcus aureus* infection, greater vegetation, and lower platelet count at diagnosis, suggesting more severe infection and a definitive indication for early surgery. Nevertheless, it is noteworthy that the time between diagnosis and surgery was similar among the 3 groups, and the ARR group eventually developed a more severe hemodynamic condition (33% of patients were intubated) before surgery. This was partly because of the prevalence of preoperative cerebral complications, especially intracranial hemorrhage, in the ARR group and patients thus had to wait weeks until valve surgery regardless of their infection with more refractory bacterial species (*Staphylococcus species*). A longer waiting period with a severe refractory infection might result in greater destruction of the aortic annulus and hemodynamic compromise, eventually requiring prolonged cardiopulmonary bypass and cardiac arrest times, and use of blood products. It is reasonable that the greater surgical invasion increased the risk of major cardiovascular events-related death or MOF-related death in the ARR group. We previously reported that early valve surgery for patients with acute stroke could be performed safely with a low incidence of neurological deterioration. Therefore, we believe that early surgical intervention should be considered in order to prevent further destruction of the aortic annulus in patients with a more refractory or invasive infection, such as *Staphylococcus* species-related endocarditis or prosthetic valve endocarditis, even if preoperative cerebral complications are present.

Although the mortality risk was high in patients with a perivalvular abscess, the level of inflammation, end-organ function, and hemolytic parameters during the first 2 months were favorable and comparable with those of patients without an abscess. The requirement for CVVHD was significantly higher in patients with a perivalvular abscess, though their renal function immediately recovered, likely because CVVHD was mainly required not for renal impairment but for heart failure caused by the longer operative time. We suspect that renal function is preserved even in patients with a severe perivalvular abscess if they survive the super-acute perioperative period. There are concerns regarding remnant infection after surgery in patients with a perivalvular abscess, because patch reconstruction or ARR separates the cavity from blood flow and antibiotics. However, though there was a slight difference in white blood cell counts and CRP levels at 4 weeks, our findings are the first to demonstrate satisfactory postoperative inflammatory change in patients with a perivalvular abscess. Reconstruction of the aortic annulus with a pericardial patch may precipitate paravalvular leakage after valve replacement, though no clear data about the incidence of paravalvular leakage after patch reconstruction have been reported. Although 11% of the patients in the PR group developed paravalvular leakage, none suffered from a hemolytic problem or heart failure, and the median serum LDH level was similar to that of patients without a perivalvular abscess. Additional evaluations are needed regarding risk factors and prognosis of patients with paravalvular leakage after aortic annulus reconstruction.

**Study Limitations**

First, because of its multicenter retrospective design, the indications and operative procedures varied slightly among the participating hospitals. Also, because of the limited number of patients with a perivalvular abscess, statistical power, especially for subset analysis between the PR and ARR groups, is lacking. However, detailed parameters for these patients at diagnosis and the perioperative period are shown. Thirdly, we could not quantitatively evaluate the severity of aortic root abscess because the procedure did not always reflect the severity of the abscess, although the severity of the abscess in the AAR group may be greater than that in the PR group. Finally, because the OSCAR database was established in 2009, we only analyzed mid-term outcomes.

In conclusion, patients treated with patch reconstruction had acceptable clinical results, but the clinical results for patients who require full ARR for severe tissue destruction are still challenging with high levels of morbidity and major cardiovascular events-related or MOF-related death.

**Conflicts of Interest**

None to declare.

**References**

1. Anguera I, Miro JM, Cabell CH, Abrutyn E, Fowler VG Jr, Hoen B, et al. Clinical characteristics and outcome of aortic endocarditis with perianular abscess in the International Collaboration on Endocarditis Merged Database. *Am J Cardiol* 2005; 96:976–983.

2. Anguera I, Miro JM, Evangelista A, Cabell CH, San Roman JA, Vilacosta I, et al. Periannular complications in infective endocarditis involving native aortic valves. *Am J Cardiol* 2006; 98: 1254–1260.

3. Leontyev S, Davierwala PM, Krogh G, Feder S, Oberbach A, Bakhtiar F, et al. Early and late outcomes of complex aortic
root surgery in patients with aortic root abscesses.  *Eur J Cardiothorac Surg* 2016; 49: 447–454; discussion 454–455.

4. Rouze S, Flecher E, Revest M, Aymami A, Roisne A, et al. Infective endocarditis with paravalvular extension: 35-year experience.  *Ann Thorac Surg* 2016; 102: 549–555.

5. Okada K, Okita Y. Surgical treatment for aortic periannular abscess/pseudoaneurysm caused by infective endocarditis.  *Gen Thorac Cardiovasc Surg* 2013; 61: 175–181.

6. Musci M, Weng Y, Hubler M, Amiri A, Pasie M, Kosky S, et al. Homograft aortic root replacement in native or prosthetic active infective endocarditis: Twenty-year single-center experience.  *J Thorac Cardiovase Surg* 2010; 139: 666–673.

7. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis.  *Clin Infect Dis* 2000; 30: 639–638.

8. Leontyev S, Borger MA, Modi P, Lehmman S, Seeburger J, Doenst T, et al. Surgical management of aortic root abscess: A 13-year experience in 172 patients with 100% follow-up.  *J Thorac Cardiovasc Surg* 2012; 143: 332–337.

9. David TE, Regesta T, Gavra G, Armstrong S, Maganti MD. Surgical treatment of paravalvular abscess: Long-term results.  *Eur J Cardiothorac Surg* 2007; 31: 43–48.

10. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rymbak MJ, et al. Infective endocarditis in adults: Diagnosis, antimicrobial therapy, and management of complications: A Scientific Statement for Healthcare Professionals from the American Heart Association.  *Circulation* 2015; 132: 1435–1486.

11. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM).  *Eur Heart J* 2015; 36: 3075–3128.

12. Yoshioka D, Sakaguchi T, Yamauchi T, Okazaki S, Miyagawa S, Nishi H, et al. Impact of early surgical treatment on postoperative neurologic outcome for active infective endocarditis complicated by cerebral infarction.  *Ann Thorac Surg* 2012; 94: 489–495; discussion 496.

13. Yoshioka D, Toda K, Sakaguchi T, Okazaki S, Yamauchi T, Miyagawa S, et al. Valve surgery in active endocarditis patients complicated by intracranial haemorrhage: The influence of the timing of surgery on neurological outcomes.  *Eur J Cardiothorac Surg* 2014; 45: 1082–1088.

**Supplementary Files**

**Supplementary File 1**

Appendix S1. Hospitals in Multicenter Study

**Figure S1.** Disposition of patients in the present study.

Please find supplementary file(s);

http://dx.doi.org/10.1253/circj.CJ-17-0355