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Clinical Research

Mid-term Outcomes in Nonelderly Adults Undergoing Surgery for Isolated Aortic Valve Infective Endocarditis: Results From Two Canadian Centers

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ABSTRACT

Background: Little is known about the mid-term prognosis of nonelderly patients (≤60 years) after the surgical treatment of isolated aortic valve infective endocarditis (IE). Better characterization of these outcomes could help in tailoring the surgical management in these patients.

Methods: From 2000 to 2015, 164 adult patients ≤60 years of age (mean 46 ± 11 years, 81% male) underwent surgical treatment for isolated aortic valve IE in 2 high-volume Canadian centers. Twenty-three patients (14%) were intravenous drug users (IVDUs). Patients with recurrent IE or concomitant endocarditis on other valves were excluded. The aortic valve was replaced with a mechanical prosthesis (44%), a tissue valve (30%), a homograft (18%), or a Ross procedure (9%). Mean follow-up was 6.2 ± 4.6 years (92% complete).

Results: Thirty-day mortality was 7%. Actuarial survival rates at 5 and 10 years were 80 ± 3% and 71 ± 4%, respectively. IVDU (hazard ratio

RÉSUMÉ

Introduction : On en connaît peu sur le pronostic à moyen terme des patients non âgés (≤ 60 ans) après le traitement chirurgical de l'endocardite infectieuse (EI) isolée de la valve aortique. Une meilleure caractérisation de ces résultats pourrait aider à adapter la prise en charge chirurgicale à ces patients.

Méthodes : De 2000 à 2015, 164 patients adultes ≤ 60 ans (moyenne de 46 ± 11 ans, 81 % d'hommes) ont subi un traitement chirurgical pour l'EI isolée de la valve aortique dans 2 établissements canadiens très fréquentés. Vingt-trois patients (14 %) étaient des utilisateurs de drogues par injection (UDI). Les patients ayant eu une EI récidivante ou une endocardite concomitante sur d'autres valves ont été exclus. La valve aortique a été remplacée par une prothèse mécanique (44 %), une valve tissulaire (30 %), une homogreffe (18 %) ou une intervention de Ross (9 %). Le suivi moyen était de 6,2 ± 4,6 ans (92 % terminé).

Nearly 40% of all cases of infective endocarditis (IE) present with isolated aortic valve endocarditis.[1] Despite optimal medical therapy, up to one-half of patients will require surgical intervention for complete removal of all infected tissues.[2,3] To this day, periprocedural issues, including optimal timing of surgery and management of patients presenting with strokes, have been the focus in the literature.[4,5] In addition, most studies include patients of all ages and a mix of left- and right-side IE. Although older age has been identified as a predictor of mortality in patients with IE,[6,7] there is a lack of data regarding outcomes in nonelderly patients (≤60 years of age). Specifically, one of the issues that has not yet been addressed is the mid-term prognosis of this patient group after they have undergone surgical treatment of aortic valve IE.

Younger patients present specific characteristics and considerations that are unique to their age group. Longer anticipated life expectancy, compliance issues that may complicate anticoagulation management, and faster rates of tissue valve degeneration all need to be considered when choosing the type of aortic valve substitute. In patients ≤60 years of age, a range of surgical options might be considered, which may vary considerably in terms of operative time and complexity, ranging from isolated aortic valve replacement (AVR) to a

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[HR] 3.8, 95% CI 1.4-10.1; $P = 0.01$) and prosthetic valve endocarditis (HR 2.6, 95% CI 1.1-6.4; $P = 0.04$) were associated with increased mid-term mortality. Mid-term survival was best in non-IVDU patients with native valve endocarditis, yet lower than a matched elective aortic valve replacement (AVR) population. Overall, freedom from recurrence of IE at 1, 5, and 10 years was 94 ± 2%, 91 ± 3%, and 89 ± 3%, respectively. IVDU was associated with higher rates of recurrence, especially in the first year after surgery.

Conclusions: In nonelderly adults undergoing surgery for aortic valve IE, mid-term survival is suboptimal. Although non-IVDU patients with native valve endocarditis have better mid-term outcomes, survival remains lower than a matched population of elective AVR in nonelderly patients.

Résultats : La mortalité après 30 jours était de 7 %. Les taux actuariels de survie après 5 ans et 10 ans étaient respectivement de 80 ± 3 % et de 71 ± 4 %. L'UDI (rapport de risque [RR] 3,8, intervalles de confiance [IC] à 95 % 1,4-10,1 ; $P = 0,01$) et l'endocardite sur prothèse valvulaire (RR 2,6, IC à 95 % 1,1-6,4 ; $P = 0,04$) ont été associées à une augmentation de la mortalité à moyen terme. Les taux de survie à moyen terme étaient supérieurs chez les patients non-UDI ayant une endocardite sur valve native, mais plus bas que dans la population appariée ayant subi un remplacement de la valve aortique (RVA) non urgent. Dans l'ensemble, l'absence de récidive de l'EI après 1 an, 5 ans et 10 ans était respectivement de 94 ± 2 %, de 91 ± 3 % et de 89 ± 3 %. L'UDI était associée à des taux plus élevés de récidive, particulièrement dans la première année après l'intervention chirurgicale.

Conclusions : Chez les adultes non âgés qui subissent une intervention chirurgicale de l'EI de la valve aortique, la survie à moyen terme est sous-optimale. Bien que les patients non-UDI ayant une endocardite de la valve native aient de meilleurs résultats à moyen terme, les taux de survie demeurent plus faibles que dans la population appariée de RVA non urgent chez les patients non âgés.

total root replacement with the use of a homograft or a pulmonary autograft (Ross procedure). It has previously been suggested that IE is a chronic condition, with late prognosis closer to that of patients with end-stage renal failure or after mediastinal radiation therapy.[8,9] However, most of those studies included older patients or those with multivalve infection. Therefore, careful understanding of the mid-term outcomes of nonelderly adults after aortic valve or root surgery for isolated aortic valve IE could help to better individualize treatment and guide postoperative follow-up.

The primary aim of the present study was to determine the mid-term survival of nonelderly adults (≤60 years of age) undergoing surgery for isolated aortic valve IE. Furthermore, comparison to nonelderly patients undergoing elective AVR during the same study period was performed with the use of propensity-matched analyses. The secondary objectives were to determine the rate of recurrence of IE and to identify predictors of mortality.

Methods

Patient population

From 2000 to 2015, 164 consecutive patients 18-60 years of age underwent surgical treatment for isolated native or prosthetic aortic valve IE at 2 high-volume academic centers: the Montreal Heart Institute (100 patients) and the Institut de Cardiologie et de Pneumologie de Québec (64 patients). Patients requiring concomitant nonvalvular interventions and those with first-time prosthetic valve endocarditis (PVE) were included. Also, patients with isolated aortic valve IE and periaortic abscess requiring reconstruction of the aortic-mitral continuity and limited repair of the anterior leaflet of the mitral valve through the aorta were included. However, patients with recurrent aortic valve IE or concomitant IE on other valves requiring multiple valve surgery were excluded. Patients were identified in the databases of both centers. Charts were reviewed to collect demographic data, to confirm the diagnosis of IE, and to review surgical protocol. IE was diagnosed with the use of the modified Duke criteria.[10] Stroke and transient ischemic attack (TIA) were diagnosed according to the American Heart Association/American Stroke Association definition.[11] Stroke or TIA occurring within 2 weeks after surgical intervention was defined as "recent."

Control group

A control group of patients 18-60 years of age who underwent AVR from 2000 to 2015 at the participating institutions was used for comparison purposes. A total of 1171 patients were included: 431 bioprostheses, 536 mechanical prostheses, 164 Ross procedures, and 40 aortic homografts. Preoperative and intraoperative data were prospectively collected into preexisting institutional valve databases. Survival status at the time of study closure was obtained for all patients. A propensity score was calculated to match patients undergoing AVR for endocarditis with those undergoing elective AVR according to the year of surgery, age, sex, preoperative creatinine level, diabetes, coronary artery disease, preoperative ejection fraction, and the type of valve replacement they received. The control group included a total of 223 patients). Patients were matched using the nearest neighbour method and a caliper width equal to 0.2 (Supplemental Table S1).

This study was approved by the Institutional Review Board, and requirement for individual patient consent was waived. All operative protocols were reviewed to confirm the type of valve procedure, the presence of a periannular abscess, the extension of the infection, and valve phenotypes. Patient charts were all retrospectively reviewed. The mean follow-up period was 6.2 ± 4.6 years and was 92% complete within 6 months after study closure.

Surgical technique

Timing of surgery was dictated by the patient's clinical condition and any history of preoperative stroke. The decision was individually made among surgery, cardiology, and infectious disease teams. Whenever clinically possible, surgery was

Table 1. Preoperative characteristics of nonelderly patients undergoing surgery for isolated aortic infective endocarditis (n = 164 patients)

Characteristic	Result
Age (y), mean ± SD	46.4 ± 10.7
Sex female	32 (20%)
IV drug user	23 (14%)
Diabetes	23 (14%)
Dyslipidemia	53 (33%)
Hypertension	47 (29%)
NYHA > 2	73 (45%)
Bicuspid valve	40 (24%)
Prosthetic valve endocarditis	46 (28%)
Causative agent	
Streptococcus	52 (32%)
Staphylococcus aureus	35 (21%)
Staphylococcus epidermidis	15 (9%)
Enterococcus	15 (9%)
Haemophilus	5 (3%)
Other	19 (12%)
Unknown	23 (14%)
Previous stroke/TIA	31 (19%)
Recent stroke/TIA	19 (12%)
Hemodialysis	4 (2%)
Permanent pacemaker	7 (4%)
CAD	15 (9%)
LVEF (%), mean ± SD	56.8 ± 9.7
Aortic insufficiency ≥ 2	113 (69%)

Unless otherwise specified, results are presented as n (%).

CAD, coronary artery disease, IV, intravenous, LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class.

delayed up to 14 days in patients with preoperative stroke to reduce the risk of hemorrhagic transformation. The choice of operative technique and valve substitute was a shared decision between the endocarditis team and the patient based on preoperative characteristics and surgeon experience and preference. The guiding principles for surgical therapy were removal of any foreign or prosthetic material, radical debridement of all infected tissues and cavities, removal of potential sources of embolism, and restoration of valve function. All patients received intravenous antibiotics for 6-8 weeks after surgery.

Statistical analyses

Continuous variables are presented as mean ± SD or median (interquartile range [IQR]) as appropriate. Categoric variables are reported as n (%). Survival curves were produced with the use of the Kaplan-Meier method and compared by means of log-rank test. Expected survival of an age- and sex-matched population was obtained with the use of the Hakulinen method.[12] The estimated age-, sex-, and year of surgery—matched population survival curve was graphically compared with the population of this study. Cox regression analyses were used to determine predictors of mid-term mortality. The predictors of mortality are presented as hazard ratio (HR) with 95% confidence interval (CI). Recurrences of endocarditis were analysed with the use of competing risk regressions. The cumulative incidence functions were compared with the use of the Gray-Fine regression model. The significance level used for the analyses was 0.05. All statistical analyses were performed with the use of Stata version 14 (StataCorp, College Station, TX).

Table 2. Perioperative outcomes of nonelderly patients undergoing surgery for isolated aortic infective endocarditis (n = 164 patients)

Outcome	Result
AVR	112 (68%)
Mechanical	63 (38%)
Biological	49 (30%)
Bentall	38 (23%)
Homograft	29 (18%)
Mechanical	9 (5%)
Ross procedure	14 (9%)
Concomitant procedures	
MV repair	20 (12%)
CABG	16 (10%)
TVR	8 (5%)
VSD closure	3 (2%)
Hemi-arch reconstruction	2 (1%)
PFO closure	2 (1%)
Hemi-Cabrol procedure	2 (1%)
Myectomy	2 (1%)
Others	6 (4%)
CPB time (min), mean ± SD	141 ± 78
Aortic cross-clamp time (min), mean ± SD	108 ± 56
Periannular abscess	64 (39%)
Use of pericardial patch to close an abscess cavity	37 (23%)
Postoperative complications	
New PM implantation	15 (9%)
Reoperation for bleeding	13 (8%)
Pulmonary infection	13 (8%)
Stroke	6 (4%)
30-day mortality	11 (7%)
MOF	4 (2.4%)
Intraoperative deaths	3 (1.8%)
Sudden cardiac death	3 (1.8%)
Cardiogenic shock	1 (0.6%)

Unless otherwise specified, results are presented as n (%).

AVR, aortic valve replacement, CABG, coronary artery bypass grafting, CPB, cardiopulmonary bypass, MOF, multiorgan failure, MV, mitral valve, PFO, patent foramen ovale, PM, pacemaker, TVR, tricuspid valve repair, VSD, interventricular septal defect.

Results

Preoperative data

Patient characteristics are listed in Table 1. Mean age of the cohort was 46 ± 11 years (81% male). Twenty-three patients (14%) were intravenous drug users (IVDUs). Among the IVDUs, 13 had a biologic AVR, 4 underwent valve replacement with the use of a homograft, 4 had a mechanical AVR, and 1 underwent a Ross procedure. Of all 164 patients, 118 (72%) had native valve endocarditis (NVE) and the rest had PVE (28%). A total of 19 patients (12%) presented with a new stroke or TIA. Euroscore II for the cohort was 10.3 ± 9.4%. The median delay between diagnosis and surgery was 8 days (range 0-42 days, IQR 3.5-22.0). *Streptococcus* and *Staphyloccocus aureus* were isolated in 32% and 21% of cases, respectively.

Operative outcomes

One hundred twelve patients (68%) underwent conventional AVR (63 mechanical, 49 biologic), and 38 patients (23%) underwent total aortic root replacement with coronary reimplantation (29 homograft, 9 mechanical). In addition, 14 patients (9%) had a Ross procedure. Euroscore II was higher

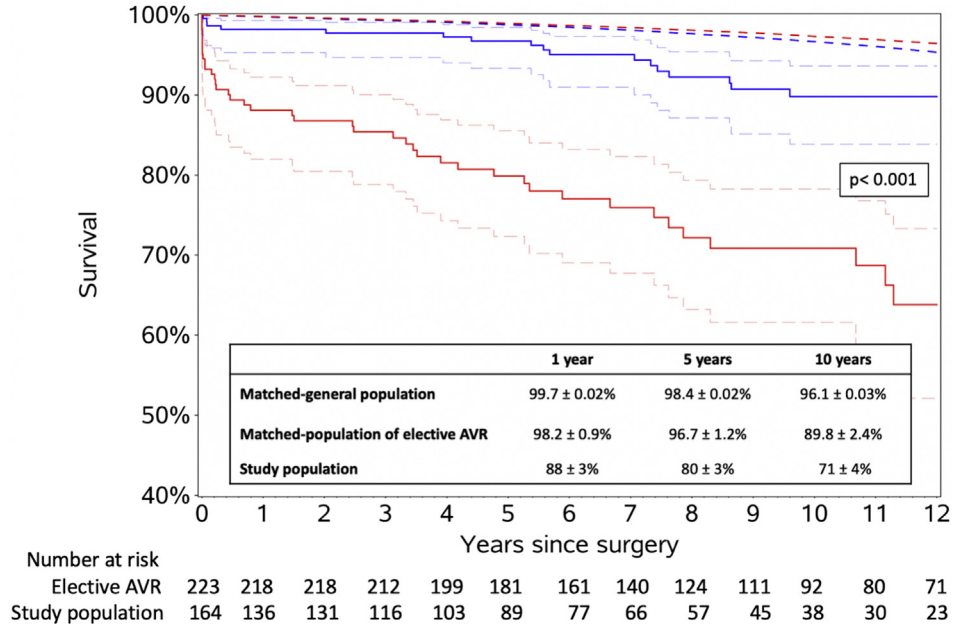

Figure 1. Mid-term survival of patients undergoing surgery for isolated aortic valve infective endocarditis (**red**) versus a matched population of patients undergoing elective aortic valve replacement (AVR; **blue**) versus the age- (**dashed red**) and sex- (**dashed blue**) matched general population.

for homograft (15.2%) compared with mechanical (10.2%), biologic (8.1%) ,or Ross procedure (7.7%; $P = 0.008$). Aortic abscesses were found in 64 patients (39%). They were repaired either primarily (n = 27) or with the use of an autologous or bovine pericardial patch (n = 37).

Eleven patients (6.7%) died within 30 days after surgery (Table 2). As predicted, observed 30-day mortality was higher for homograft (20.8%) compared with mechanical (5.9%), biologic (2.1%) ,or Ross procedure (0%; $P = 0.03$). In addition, surgery for PVE was associated with higher 30-day mortality (17.4%) than surgery for NVE (1.7%; $P = 0.001$). Six patients (4%), all of whom had no preoperative stroke or TIA, suffered from a neurologic event after surgery. None of the patients with preoperative stroke or TIA had worsening of their neurologic condition.

Mid-term survival

Overall, 42 patients (26%) died during the study period. Survival rates at 1, 5, and 10 years were 88 ± 3%, 80 ± 3%, and 71 ± 4%, respectively (Fig. 1), which is lower than the age-, sex-, and year of surgery—matched Québec general population undergoing elective AVR. In propensity-matched analysis, survival was lower compared with patients undergoing elective AVR ($P < 0.001$; Fig. 1). IVDU (HR = 3.8, 95% CI 1.4-10.1; $P = 0.01$) and PVE (HR = 2.6, 95% CI 1.1-6.4, $p = 0.04$) were associated with higher mid-term mortality.

Compared with patients with NVE, those undergoing surgery for PVE had lower survival, which was maintained up to 10 years after surgery. Survival rates after surgery for isolated PVE at 1, 5, and 10 years were 72 ± 7%, 64 ± 7%, and 60 ± 8%, respectively, versus 95 ± 2%, 86 ± 3%, and 75 ± 5%, respectively after surgery for NVE ($P = 0.005$; Fig. 2A). IVDU patients had significantly worse mid-term survival compared with non-IVDU patients. In IVDU patients, survival rates at 1, 5, and 10 years were 69 ± 1%, 58 ± 1%, and 33 ± 1%, respectively, versus 91 ± 2%, 86 ± 3%, and 77 ± 4% in non-IVDU patients ($P < 0.001$). Figure 2, B and C, depicts 10-year survival of patients after surgery according to their IVDU status and whether they had NVE or PVE. Non-IVDU patients with NVE had the highest 10-year survival (82.2 ± 5%; $P < 0.001$). Nevertheless, this was lower than that of the matched control group ($P = 0.02$; Supplemental Fig. S1). There were no differences in mid-term survival rates among the different valve substitutes ($P = 0.16$) and different techniques ($P = 0.65$).

Recurrence of infective endocarditis

A total of 14 patients (9%) had documented recurrence of IE during the study period. Overall, freedom from recurrence at 1, 5, and 10 years was 94 ± 2%, 91 ± 3%, and 89 ± 3%, respectively (Fig. 3A). Among patients with recurrence, 9 occurred within the first year after surgery (64%). The median time to recurrence of IE was 4 months (range 0.5-113 months, IQR 25-74 months). All patients with recurrence of IE were treated with the use of intravenous (IV) antibiotics and 7 of them had a redo procedure. Two patients died shortly after recurrence of endocarditis (1 had undergone surgery and 1 had been treated with antibiotics only). Of the 7 patients who did not undergo reoperation, 1 had a mobile mass on the mitral valve detected on 1-month follow-up echocardiography. The patient was still on IV antibiotics and had negative blood cultures. It was decided to continue the antibiotic treatment and perform follow-up echocardiography, which was negative for any residual signs of endocarditis. Two patients had positive blood cultures within 1 month after surgery. Their echocardiograms could not clearly identify any vegetation. Antibiotic treatment was continued and blood cultures were subsequently repeated and came back negative. One non-IVDU patient who initially presented with

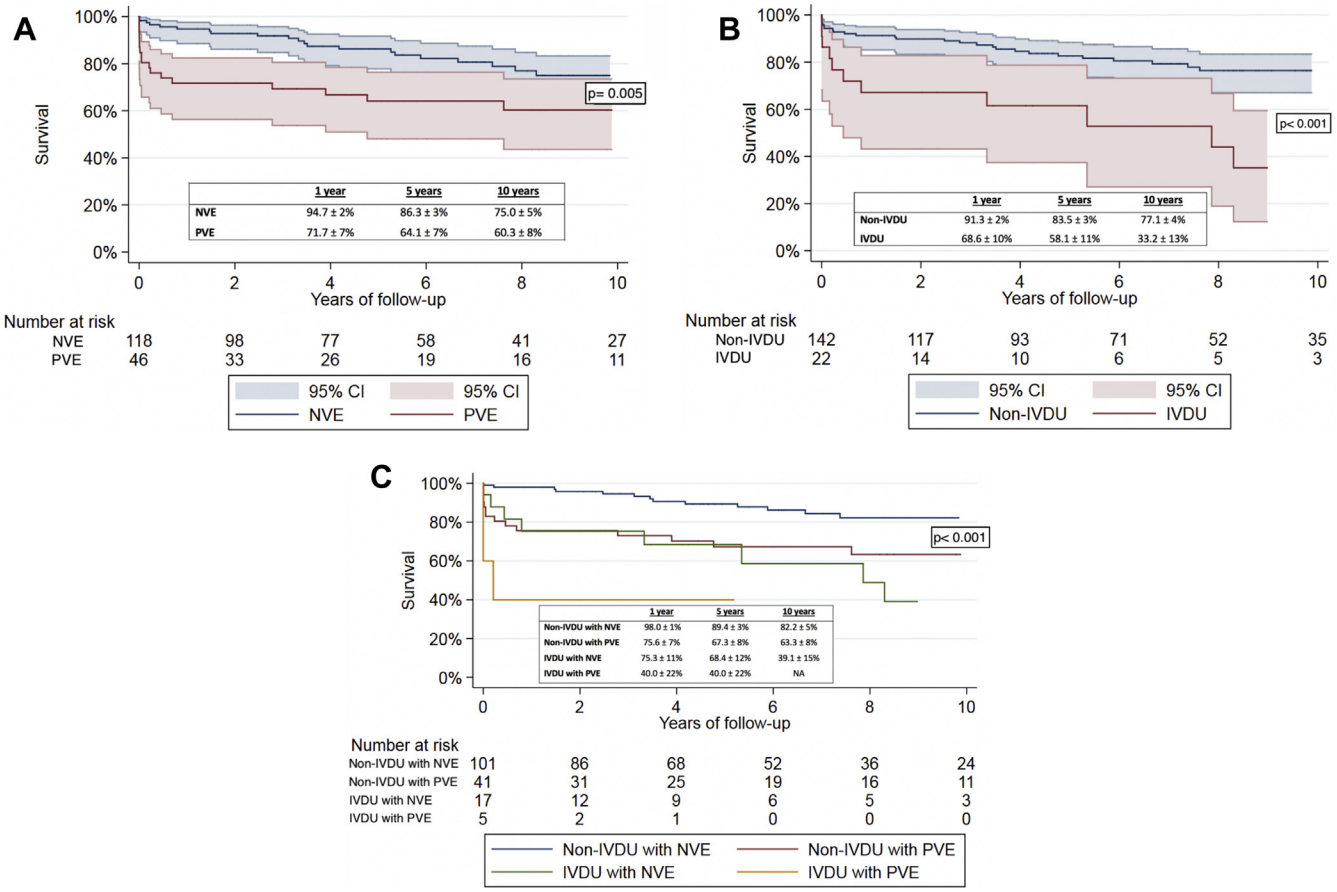

Figure 2. (**A**) Mid-term survival in patients undergoing surgery for isolated aortic native valve endocarditis (NVE; **blue**) versus prosthetic valve endocarditis (PVE; **red**). (**B**) Mid-term survival in non− intravenous drug user (IVDU; **blue**) versus IVDU (**red**) patients undergoing surgery for isolated aortic infective endocarditis (IE). (**C**) Mid-term survival in patients undergoing surgery for isolated aortic IE according to their non-IVDU/IVDU and NVE/PVE status (non-IVDU with NVE: **blue**; non-IVDU with PVE: **red**; IVDU with NVE: **green**; IVDU anwithd PVE: **yellow**). CI, confidence interval.

a *Staphylococcus lugdunensis* NVE had recurrence 2 months after surgery (2 weeks after stopping antibiotics) and presented with severe neurologic deficit. Blood cultures were positive for *Staphylococcus lugdunensis* and *Pseudomonas aeruginosa*. A multidisciplinary decision was taken with the patient and his family to adopt a conservative approach. The patient had a good response to the antibiotic treatment, did not need reoperation, and had substantial neurologic improvement. One patient died in septic shock before redo surgery could be performed. One patient was an IVDU patient who developed 2 recurrences during the study period. Antibiotic treatment was initiated for the first recurrence. The patient had a second recurrence 3 months later and died of septic complications. Finally, 1 patient had pulmonary homograft endocarditis 3 years after a Ross procedure for aortic valve endocarditis, with a different infecting organism. He underwent successful treatment with the use of IV antibiotics. While awaiting a transcatheter procedure for pulmonary valve regurgitation, he died at home from a drug overdose.

Cumulative incidence of recurrence of IE, with mortality as a competing risk, was similar between patients with NVE versus PVE ($P = 0.50$; Fig. 3B). A total of 3 patients with PVE had a recurrence (1 mechanical AVR, 1 biologic AVR, 1 homograft). The cumulative incidence of recurrence in IVDU and non-IVDU patients was similar ($P = 0.30$). The difference was mostly observed during the first year after surgery, after which the curves were very similar (Supplemental Fig. S2). Cumulative incidence of recurrence was similar when comparing NVE in non-IVDU patients with the other subgroups ($P = 0.51$; Supplemental Fig. S3). Nevertheless, at 10 years, survival free from recurrence was higher in non-IVDU patients with NVE ($P = 0.001$; Supplemental Fig. S4). Table 3 summarizes the mid-term outcomes of nonelderly adults operated on for aortic valve IE.

Discussion

In this series, we have shown that overall mid-term survival after surgical treatment of isolated aortic valve IE in nonelderly adults (≤ 60 years of age) is lower than that in the matched general population and that of patients undergoing elective AVR. The presence of IVDU and PVE emerge as 2 important determinants of mid-term survival. In non-IVDU patients with NVE, mid-term survival compares favourably with outcomes reported after isolated elective AVR in a similar age group. We had previously examined outcomes of isolated elective AVR with the use of mechanical or biologic prostheses in this nonelderly patient population with the exclusion of

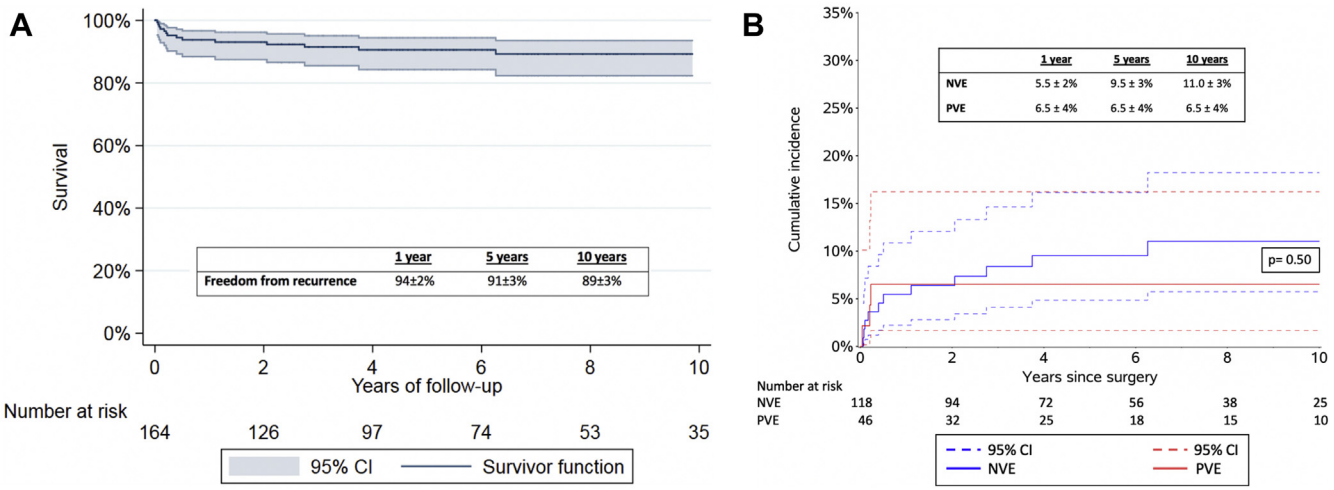

Figure 3. (**A**) Freedom from recurrence in nonelderly patients undergoing surgery for isolated aortic valve IE (**blue**). (**B**) Cumulative incidence of recurrence of endocarditis with mortality as a competing risk in patients with NVE (**blue**) versus PVE (**red**) undergoing surgery for isolated aortic valve IE. Abbreviations as in Figure 2.

endocarditis, and at 10 years, survival ranged from 79% to 87%,[13,14] which was similar to other published studies examining outcomes in similar patient populations.[15,16] The present study therefore suggests that in this age group, patients with PVE or IVDU should be considered to be carrying chronic conditions with a continued impact on mid-term prognosis despite successful surgical treatment. In contrast, non-IVDU patients with NVE represent a favourable subgroup of patients, with mid-term outcomes approaching those of patients undergoing elective surgery.

Another important finding from this study is that patients should be followed very closely during the first year after surgery for aortic valve IE. The differences in both survival between PVE and NVE patients and cumulative incidence of recurrence observed in IVDU versus non-IVDU patients were most pronounced in the first year after surgery. This highlights 2 key elements in the management of these patients. First, the treatment of patients with IVDU should include close monitoring and referral to a rehabilitation program to maximize the likelihood of abstinence and reduce the risk of recurrence of infection through the use of the permanent IV catheter. A social worker, psychologist, or psychiatrist should be an integral part of the multidisciplinary endocarditis team to ensure optimal results after surgical intervention in these patients. Although this can be a challenging patient population, dedicated efforts to encourage abstinence and curb recurrences could prove to be medically beneficial and cost-effective for health care systems. Such models of care have been successfully implemented in other Canadian centers, and we are currently working toward such a goal to optimize outpatient follow-up and abstinence. As shown in our results, cumulative incidence of recurrences differs little between IVDU and non-IVDU patients after 1 year, although this may be due to a selection bias due to attrition of the more severe cases. The optimal type of valve replacement remains a challenging question in young IVDU patients. Specifically, in IVDU patients, the use of mechanical prostheses should be weighed against the potential lack of compliance to lifelong anticoagulation. Nevertheless, whenever possible, the choice of prosthesis should take patient values and preferences into account.

Second, findings from this study suggest that patients with PVE should be followed very closely during the first year after surgery, similarly to the recommended follow-up regimens proposed for patients after acute type A aortic dissection.[17,18] A monitoring program consisting of serial echocardiography and positron emission tomography during the first year after surgery should be considered to detect and intervene more readily (mainly by prolonging antibiotic treatment duration) in patients with suspected recurrence of infection, those with incomplete removal of infection, and those with persistent ectopic loci of infection from previous septic emboli. Although the overall freedom from diagnosed recurrence at 1 year was 94%, there was a significant survival difference at 1 year between patients undergoing surgery for

Table 3. Mid-term outcomes of nonelderly patients undergoing surgery for isolated aortic infective endocarditis (n = 164 patients)

Outcome	n (%)
Long-term mortality (> 30 days)	31 (19%)
Unknown cause	16 (52%)
Cardiac cause	4 (13%)
Endocarditis	3 (10%)
Respiratory failure	2 (6%)
Malignancy	1 (3%)
Murder	1 (3%)
Septicemia	1 (3%)
Hemorrhagic shock	1 (3%)
MOF	1 (3%)
Drug overdose	1 (3%)
Recurrence of IE	14 (9%)
Reintervention	22 (13%)
Endocarditis	7 (32%)
Pseudoaneurysm	6 (27%)
Valve degeneration	4 (18%)
Aortic stenosis	3 (14%)
CABG	2 (9%)
Valve-related complications (bleeding, stroke/TIA, or embolism)	12/100 (12%)

IE, infective endocarditis; TIA, transient ischemic attack; other abbreviations as in Table 2.

PVE versus NVE. This may be due in part to an underdiagnosis of recurrence. The retrospective nature of the present study did not allow precise ascertainment of all causes of death, but it suggests that closer follow-up of these patients with the use of clinical and imaging evaluations may play an important role.

In recent years, the Ross procedure has been shown to provide excellent long-term outcomes in young and middle-age adults requiring AVR.[19-21] Some have even suggested that it is the best operation for adults with aortic valve stenosis and that the guidelines should be revisited.[22-24] Use of the Ross procedure in patients with aortic valve IE may provide the unique benefit of placing a living valve substitute in the aortic position, therefore reducing the risk of reinfection compared with prosthetic material. However, the Ross procedure is a longer and more complex operation. It should therefore be considered mainly in patients with limited tissue destruction and in centers of expertise with the operation. As shown in this study, in selected patients the operation can be performed safely with excellent perioperative outcomes. Interestingly, 1 IVDU patient in the present cohort underwent a Ross procedure and presented 3 years later in advanced sepsis with recurrent endocarditis from a different organism. On echocardiography, the pulmonary autograft was intact and the endocarditis was observed only on the pulmonary homograft, and it was successfully managed medically with the use of IV antibiotics. There have been few reports specifically examining the role of the Ross procedure in endocarditis, but published studies report similar outcomes.[25,26]

Use of aortic homografts has considerably decreased over the past 2 decades. This was mainly driven by the fact that reoperations can be quite challenging because of heavy calcification of the homograft, especially in younger patients, as well as the fact that recurrence of infection is no different than observed in patients undergoing prosthetic aortic valve or root replacement. Currently, it is mainly used for patients with extensive aortic root destruction and periannular abscesses. This explains the higher operative mortality observed in patients undergoing homograft aortic root replacement in the present cohort. This inherent selection bias in the use of homografts in aortic valve IE limits the ability to examine its real impact in the long term in patients with less advanced disease. Nonetheless, we think that aortic homografts provide excellent substitutes for the aortic valve in selected patients.

This study has several limitations. Although clinical follow-up data were prospectively collected, the retrospective nature of the analysis introduces a number of potential biases inherent to the study design. In addition, information of use for this specific study was not captured prospectively, including the precise choice of surgical timing and procedure. Furthermore, the exact cause of death over the follow-up period was difficult to determine retrospectively, which limits the ability to make direct inferences relating to surgical technique. Finally, the aim of this study was to examine outcomes of patients undergoing surgical treatment of aortic valve IE. Therefore, no analyses could be done to assess the efficacy of surgical versus medical treatment. Similarly, because of the infrequent nature of this condition, "between-group" comparisons could not be performed to determine differences based on surgical strategy. However, as mentioned, that was not the objective of this study.

In conclusion, this study shows that overall mid-term survival of nonelderly adults undergoing surgical treatment of isolated aortic valve IE is suboptimal. Although in non-IVDU patients with NVE, late survival is acceptable, it nevertheless remains lower than that of a matched population of patients undergoing elective AVR. The role of more complex procedures aimed at optimizing survival while reducing the risk of recurrent endocarditis in selected patients remains to be determined. Furthermore, dedicated surveillance programs with the use of serial clinical and imaging follow-up in the first year after surgery may have a significant impact on patient outcomes, especially in patients with PVE. Finally, in IVDU patients, multidisciplinary management after discharge, with a focus on avoidance of substance abuse, is equally important in the first year. Further follow-up of these patients and evaluation of these proposed management strategies are warranted to determine their effectiveness in improving short- and long-term outcomes in nonelderly patients with aortic valve IE.

Disclosures

The authors have no conflicts of interest to disclose.

References

1. van den Brink FS, Swaans MJ, Hoogendijk MG, et al. Increased incidence of infective endocarditis after the 2009 European Society of Cardiology guideline update: a nationwide study in the Netherlands. Eur Heart J 2017;3:141-7.
2. Hoen B, Alla F, Selton-Suty C, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. JAMA 2002;288:75-81.
3. Tornos P, Iung B, Permanyer-Miralda G, et al. Infective endocarditis in Europe: lessons from the Euro Heart Survey. Heart 2005;91:571-5.
4. Sultan I, Bianco V, Kilic A, Chu D, Navid F, Gleason TG. Aortic root replacement with cryopreserved homograft for infective endocarditis in the modern North American opioid epidemic. J Thorac Cardiovasc Surg 2019;157:45-50.
5. Takahashi H, Arif R, Kallenbach K, Tochtermann U, Karck M, Ruhparwar A. Surgical treatment of aortic valve endocarditis with left ventricular-aortic discontinuity. Ann Thorac Surg 2013;96:72-6.
6. Nunes MCP, Guimarães-Júnior MH, Murta Pinto PHO, et al. Outcomes of infective endocarditis in the current era: early predictors of a poor prognosis. Int J Infect Dis 2018;68:102-7.
7. Smith JM, So RR, Engel AM. Clinical predictors of mortality from infective endocarditis. Int J Surg 2007;5:31-4.
8. Ghoneim A, Bouhout I, Perrault LP, et al. Reexamining the role of surgical aortic valve replacement after mediastinal radiation therapy. Ann Thorac Surg 2017;104:485-92.
9. Thourani VH, Keeling WB, Sarin EL, et al. Impact of preoperative renal dysfunction on long-term survival for patients undergoing aortic valve replacement. Ann Thorac Surg 2011;91:1798-807.
10. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-8.
11. Sacco RL, Kasner SE, Broderick JP, et al; An updated definition of stroke for the 21st century. A statement for healthcare professionals from the

American Heart Association/American Stroke Association. Stroke 2013;44:2064-89.

12. Hakulinen T. Cancer survival corrected for heterogeneity in patient withdrawal. Biometrics 1982;38:933-42.

13. Bouhout I, Stevens L-M, Mazine A, et al. Long-term outcomes after elective isolated mechanical aortic valve replacement in young adults. J Thorac Cardiovasc Surg 2014;148:1341-6.e1341.

14. Forcillo J, El Hamamsy I, Stevens L-M, et al. The perimount valve in the aortic position: twenty-year experience with patients under 60 years old. Ann Thorac Surg 2014;97:1526-32.

15. Bourguignon T, Lhommet P, El Khoury R, et al. Very long-term outcomes of the Carpentier-Edwards Perimount aortic valve in patients aged 50-65 years. Eur J Cardiothorac Surg 2016;49:1462-8.

16. Goldstone AB, Chiu P, Baiocchi M, et al. Mechanical or biologic prostheses for aortic-valve and mitral-valve replacement. N Engl J Med 2017;377:1847-57.

17. Erbel R, Aboyans V, Boileau C, et al; 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases. Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2873-926.

18. Hiratzka LF, Bakris GL, Beckman JA, et al. ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. J Am Coll Cardiol 2010 2010;55:e27-129.

19. El-Hamamsy I, Eryigit Z, Stevens L-M, et al. Long-term outcomes after autograft versus homograft aortic root replacement in adults with aortic valve disease: a randomised controlled trial. Lancet 2010;376(9740):524-31.

20. Mazine A, El-Hamamsy I, Verma S, et al. Ross procedure in adults for cardiologists and cardiac surgeons. J Am Coll Cardiol 2018;72:2761-77.

21. Mazine A, Rocha RV, El-Hamamsy I, et al. Ross procedure vs mechanical aortic valve replacement in adults: a systematic review and meta-analysis. JAMA Cardiol 2018;3:978-87.

22. Ouzounian M, Mazine A, David TE. The Ross procedure is the best operation to treat aortic stenosis in young and middle-aged adults. J Thorac Cardiovasc Surg 2017;154:778-82.

23. Misfeld M, Borger MA. The Ross procedure: time to reevaluate the guidelines. J Thorac Cardiovasc Surg 2019;157:211-2.

24. El-Hamamsy I, Bouhout I. The Ross procedure: time for a hard look at current practices and a reexamination of the guidelines. Ann Transl Med 2017;5:142.

25. Ringle A, Richardson M, Juthier F, et al. Ross procedure is a safe treatment option for aortic valve endocarditis: long-term follow-up of 42 patients. Int J Cardiol 2016;203:62-8.

26. Ratschiller T, Sames-Dolzer E, Paulus P, et al. Long-term evaluation of the Ross procedure in acute infective endocarditis. Semin Thorac Cardiovasc Surg 2017;29:494-501.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.06.027.