

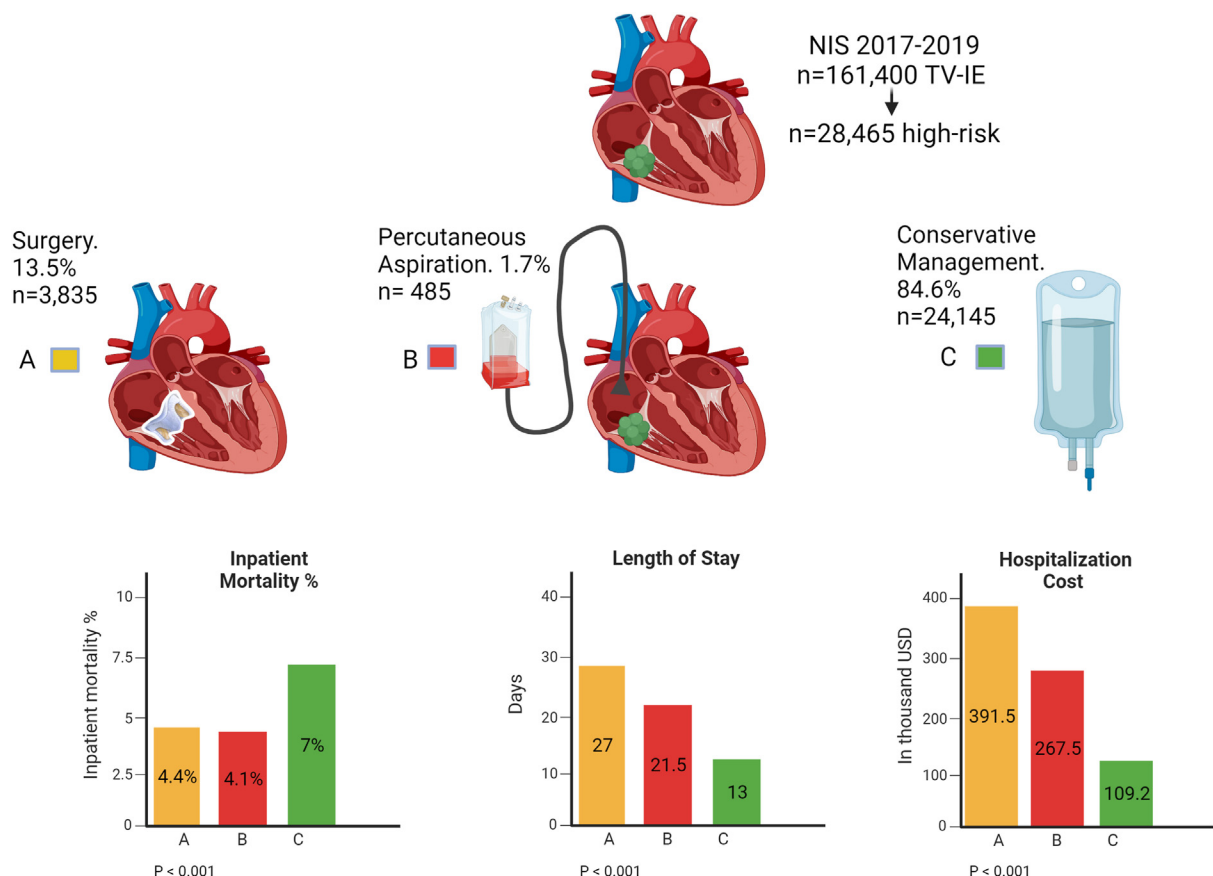
Original Article

Outcome of Percutaneous and Surgical Management for Tricuspid Infective Endocarditis: Insights From a National Study

Abdulrahman S. Museedi, MD,^a Abbas Alshami, MD,^b Sireesha Upadhrasta, MD,^a Daniela Urina-Jassir, MD,^a Ali Alsaad, MD,^a and Zach Rozenbaum, MD^a

^a Section of Cardiology, John W. Deming Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana, USA

^b Division of Cardiology, Jersey Shore University Medical University, Neptune, New Jersey, USA



ABSTRACT

Background: The prevalence of infective endocarditis (IE) and its associated mortality rates remain high, despite medical advances. In recent years, treatment options for IE have expanded, but they are yet to be widely utilized. The current study aimed to compare in-hospital

RÉSUMÉ

Contexte : La prévalence de l'endocardite infectieuse et le taux de mortalité qui y est associé demeurent élevés, malgré les progrès de la médecine. Depuis quelques années, les options thérapeutiques pour l'endocardite infectieuse sont plus nombreuses, mais elles ne sont pas

outcomes of high-risk tricuspid valve (TV) IE patients, by treatment strategy.

Methods: Patients from the National Inpatient Sample 2017-2019 database who had TV IE were grouped by therapy type—percutaneous aspiration, surgical, or conservative management. Patients were considered to be at high risk if they underwent mechanical intervention or if they had right ventricle failure or septic emboli.

Results: The analyzed cohort consisted of 28,495 patients—1.7% were treated with percutaneous aspiration, 13.5% with surgery, and 84.6% conservatively. Patients treated with percutaneous aspiration had the highest prevalence of septic shock and acute respiratory failure ($P < 0.001$). The overall in-hospital mortality rate was 7%. Patients treated conservatively had higher in-hospital mortality rates (7.5%) compared to those of the surgical group (4.4%) and the percutaneous aspiration group (4.1%; $P < 0.001$). In a multivariate analysis, conservative management was associated with an increased risk of in-hospital mortality (odds ratio 2.853, 95% confidence interval 1.748-4.659, $P < 0.001$), and no significant difference was found between the aspiration and surgical groups ($P = 0.346$). Benefits were pronounced in younger patients and those with septic shock or respiratory failure. Patients in the aspiration group had the highest rate of home discharge with self-care, of the various patient dispositions ($P < 0.001$).

Conclusions: Among high-risk patients with TV IE, an invasive approach is associated with a significantly lower in-hospital mortality rate than is a conservative approach, particularly in younger and unstable patients.

encore largement utilisées. L'étude visait à comparer les issues observées à l'hôpital par stratégie thérapeutique chez les patients atteints d'endocardite infectieuse de la valve tricuspide présentant un risque élevé.

Méthodologie : Des patients de la base de données National Inpatient Sample 2017-2019 qui étaient atteints d'endocardite infectieuse de la valve tricuspide ont été regroupés par type de traitement — aspiration percutanée, chirurgie ou prise en charge symptomatique. Les patients étaient considérés comme présentant un risque élevé s'ils avaient subi une intervention mécanique ou s'ils présentaient une insuffisance ventriculaire droite ou des embolies septiques.

Résultats : La cohorte analysée était constituée de 28 495 patients — 1,7 % d'entre eux ont été traités par aspiration percutanée, 13,5 % par chirurgie et 84,6 %, par un traitement symptomatique. La prévalence du choc septique et d'insuffisance respiratoire aiguë était la plus élevée chez les patients traités par aspiration percutanée ($p < 0,001$). Le taux de mortalité à l'hôpital global était 7 %. Le taux de mortalité à l'hôpital était plus élevé chez les patients recevant un traitement symptomatique (7,5 %) que chez ceux du groupe d'intervention chirurgicale (4,4 %) et du groupe d'aspiration percutanée (4,1 %; $p < 0,001$). Dans une analyse multivariable, la prise en charge symptomatique a été associée à un risque accru de mortalité à l'hôpital (rapport de cotes : 2,853; intervalle de confiance à 95 % : 1,748-4,659, $p < 0,001$), et aucune différence marquée n'a été observée entre les groupes d'aspiration et de chirurgie ($p = 0,346$). Les bienfaits étaient marquants chez les jeunes patients et ceux atteints d'un choc septique ou d'insuffisance respiratoire. Les patients du groupe d'aspiration affichaient le taux de congés avec auto-soins le plus élevé, parmi les différents sorts des patients ($p < 0,001$).

Conclusions : Chez les patients atteints d'endocardite infectieuse de la valve tricuspide présentant un risque élevé, une approche efficace est associée à un taux de mortalité à l'hôpital considérablement réduit par rapport à l'approche symptomatique, particulièrement chez les patients jeunes et dont l'état est instable.

The prevalence of infective endocarditis (IE) has been increasing steadily. In a national study, the incidence of IE hospitalization increased by 37% from 2003 to 2016.¹ Notably, the increase disproportionately affected younger adults, aged < 30 years, and intravenous drug users (IVDUs).¹ Despite the potential for improvement in the rate of inpatient mortality,¹ it remains high.¹⁻³ Right-side IE (RSIE) accounts for up to 10% of IE cases and occurs most frequently with IVDUs.² Although RSIE is more benign than left-side IE, it still carries a 7%-11% risk of in-hospital mortality when managed conservatively.⁴ Guidelines from the American Heart Association and the European Society of Cardiology⁵ state that the approach for RSIE should be conservative, and that surgery should be avoided when possible, due to the large percentage of IVDUs,⁶ and therefore, the risk of reinfection.² Moreover, recurrence is

linked to a decreased likelihood of survival, particularly when surgery is not feasible.² Nevertheless, for deteriorating patients, early surgical intervention may improve their prognosis.⁷

In the past, surgery was the only mechanical intervention available for IE. In recent years, use of percutaneous aspiration devices has emerged as a promising method for removal of various cardiac pathologies.⁸

Indications for surgery in RSIE include right heart failure, large tricuspid valve (TV) vegetations (≥ 20 mm), recurrent pulmonary emboli, and nonresponse to antibiotics and/or antifungal medications.⁶ Prognosis depends on several factors comprised of patient and infection characteristics,² including vegetation size,⁹ as large vegetation size is a risk factor for embolization and mortality.¹⁰ For patients deemed to be at high risk for surgical intervention, particularly in the presence of one or more of the indications, percutaneous aspiration presents a potential alternative. This approach aims to reduce vegetation size, thereby enhancing the efficacy of antimicrobial treatments in eradicating the infection, mitigating the risk of embolization, and potentially serving as a bridge to subsequent surgical intervention once the patient stabilizes. However, a point imperative to acknowledge is that percutaneous intervention carries inherent risks, including vascular or

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Corresponding author: Dr Abdulrahman S. Museedi, Tulane University School of Medicine, Section of Cardiology, 1430 Tulane Ave, Box 8548, New Orleans, Louisiana 70112, USA. Tel.: +1-504-988-5152; fax: +1-504-988-4237.

E-mail: amuseedi@tulane.edu

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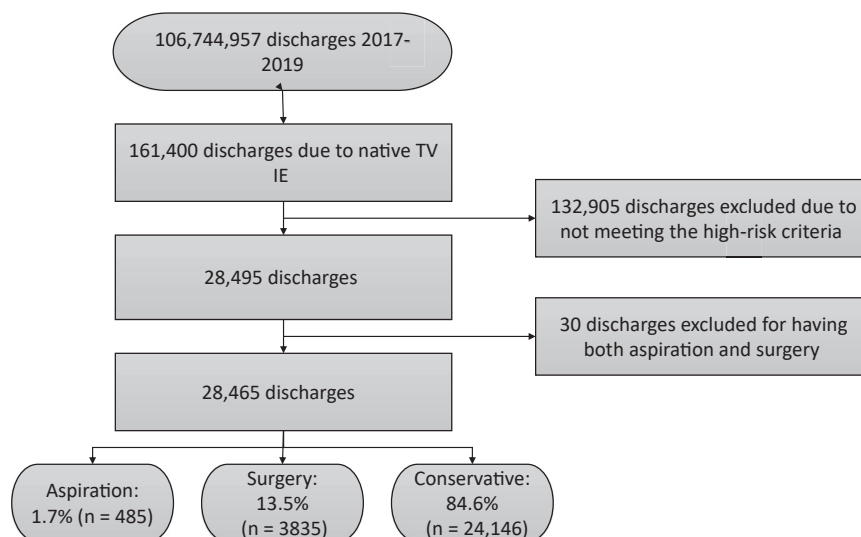


Figure 1. The flowchart of patient selection. TV IE, tricuspid valve infective endocarditis.

myocardial injury, TV damage, tamponade, and the possibility of pulmonary embolisms.^{1,11}

Although percutaneous aspiration devices are applicable for similar indications,⁸ the existing evidence supporting their efficacy remains limited. In the current study, we aimed to compare outcomes of high-risk TV IE patients treated with percutaneous aspiration vs outcomes for those with surgical and conservative management, according to a large inpatient database.

Methods

Population

We conducted a retrospective cohort study design utilizing the Healthcare Cost and Utilization Project National Inpatient Sample (NIS) 2017-2019 database.¹² This database provided a well-structured sample, representing 20% of all-payer inpatient encounters throughout the US. These

Table 1. Baseline characteristics of study groups

Variable	All (n = 28,495)	Aspiration group (n = 515)	Surgery group (n = 3835)	Medical therapy group (n = 24,145)	P
Age, y	33 (28–44)	33 (28–44)	33 (28–41)	33 (28–41)	0.252
Sex, female	15,805 (55.4)	275 (56.7)	2185 (57)	13,345 (55.3)	0.124
Race					< 0.001
White	22,580 (81.9)	380 (83.5)	3035 (82.9)	19,165 (81.8)	
Black	2065 (7.4)	35 (7.7)	325 (8.9)	1705 (7.3)	
Hispanic	1770 (6.4)	25 (5.5)	190 (5.2)	1555 (6.6)	
Other	1130 (4.1)	15 (3.3)	110 (3)	1005 (4.3)	
Primary insurance					< 0.001
Medicare	2955 (10.4)	50 (10.3)	430 (11.2)	2475 (10.3)	
Medicaid	17,090 (60.1)	330 (68)	2150 (56.1)	14,610 (60.7)	
Private insurance	3305 (11.6)	35 (7.2)	630 (16.4)	2640 (11)	
Other	5040 (17.7)	70 (14.4)	620 (16.2)	4350 (18.1)	
DM	2610 (9.1)	65 (13.4)	315 (8.2)	2230 (9.2)	0.001
CKD	2700 (9.4)	40 (8.2)	510 (13.3)	2150 (8.9)	< 0.001
Obesity	2030 (7.1)	20 (4.1)	330 (8.6)	1680 (7)	< 0.001
CAD	1490 (5.2)	40 (8.2)	320 (8.3)	1130 (4.7)	< 0.001
Smoking	18,540 (65)	285 (58.8)	2195 (57.2)	16,060 (66.5)	< 0.001
Presence of PM and/or ICD	565 (1.9)	25 (5.2)	105 (2.7)	435 (1.8)	< 0.001
Alcohol abuse	1590 (5.5)	15 (3.1)	160 (4.2)	1,415 (5.9)	< 0.001
Substance abuse	21,045 (73)	350 (72.2)	2610 (68.1)	18,085 (74.9)	< 0.001
MSSA bacteremia	11,245 (39.4)	235 (48.5)	1315 (34.3)	9695 (40.2)	< 0.001
MRSA bacteremia	10,600 (37.1)	150 (30.9)	1205 (31.4)	9245 (38.3)	< 0.001
Septic shock	7250 (25.4)	200 (41.2)	1070 (27.9)	5980 (24.8)	< 0.001
Acute respiratory failure	8920 (32.3)	180 (37.1)	1400 (36.5)	7340 (30.4)	< 0.001
Acute RV failure	405 (1.4)	0 (0)	60 (1.6)	345 (1.4)	0.01
History of cardiac surgery*	1045 (3.6)	15 (2.9)	135 (3.5)	895 (3.7)	0.55
History of systolic heart failure	1470 (5.7)	45 (8.7)	310 (8.1)	1115 (4.6)	< 0.001

Values are frequency (%) or median (interquartile range), unless otherwise indicated.

CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; ICD, implantable cardiac defibrillator; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; PM, pacemaker; RV, right ventricular.

* Cardiac surgery included coronary bypass grafting and congenital corrections.

encounters were chosen methodically by the Agency for Healthcare Research and Quality (AHRQ) to ensure that they accurately reflect all hospitalizations at the national level.

We defined high-risk patients with TV IE as any patients who underwent surgery or transcatheter vegetation aspiration, and any patients who were treated conservatively and had their course complicated by right-ventricle (RV) failure or septic emboli. Patients were divided into 3 arms, as follows: a percutaneous aspiration group, a surgical group, and a conservative group (see [Supplemental Appendix S1](#) for the International Classification of Diseases (ICD) codes used to identify these patients).

Patients included in the cohort were aged 18-100 years, had a primary admission diagnosis of acute IE of the TV, and one of the following high-risk features: (i) had undergone TV surgery; (ii) had undergone percutaneous aspiration; (iii) had developed septic emboli or RV failure. Patients were excluded if they had a prosthetic TV or a history of TV repair, had IE involving valves other than the TV, or had undergone both percutaneous aspiration and TV surgery (see [Fig. 1](#)).

Outcomes

The primary endpoint was in-hospital mortality. The secondary endpoints were the length of stay in the hospital, the cost of the hospital stay in each arm, and patient disposition.

Statistical analysis

The normality of the NIS data was assessed using the Shapiro-Wilk test. Continuous nonparametric data are reported as medians with interquartile ranges (IQRs), and categorical data are presented as frequencies and percentages. The χ^2 test was used to compare categorical variables, and

the Kruskal-Wallis test to compare continuous nonparametric variables. A multivariable logistic regression model was adjusted for baseline characteristics. A correlation matrix was constructed and analyzed for multicollinearity. A logistic regression model with the primary endpoint as the dependent variable was used in each subgroup, to assess whether the subgroup favours intervention (aspiration or surgery) vs medical therapy. Subgroups assessed included those grouped by age, gender, presence of septic shock, presence of respiratory failure, and substance use. An alpha (P) value of 0.05 was considered statistically significant. SPSS Statistics, version 25.0 (IBM, Armonk, NY), was used for all statistical analyses.

Results

Baseline characteristics

A total of 106,744,957 discharges were screened, and isolated native TV IE was found in 161,400 patients. Of these, 28,495 were identified as having a high level of risk according to the above-specified criteria ([Fig. 1](#)). Notably, 30 patients were excluded because they underwent both aspiration and surgery during the same admission. None had RV failure, but most had septic emboli (66.7%) and a history of substance use disorder (83.3%). Among those 30 patients, no in-hospital mortality occurred ([Supplemental Table S1](#)).

Among patients included in the analysis, 1.7% ($n = 485$) were treated with percutaneous aspiration, 13.5% ($n = 3835$) underwent surgery, and 84.6% ($n = 24,145$) were treated conservatively. Baseline characteristics of the study groups are presented in [Table 1](#). The median age of the entire cohort was

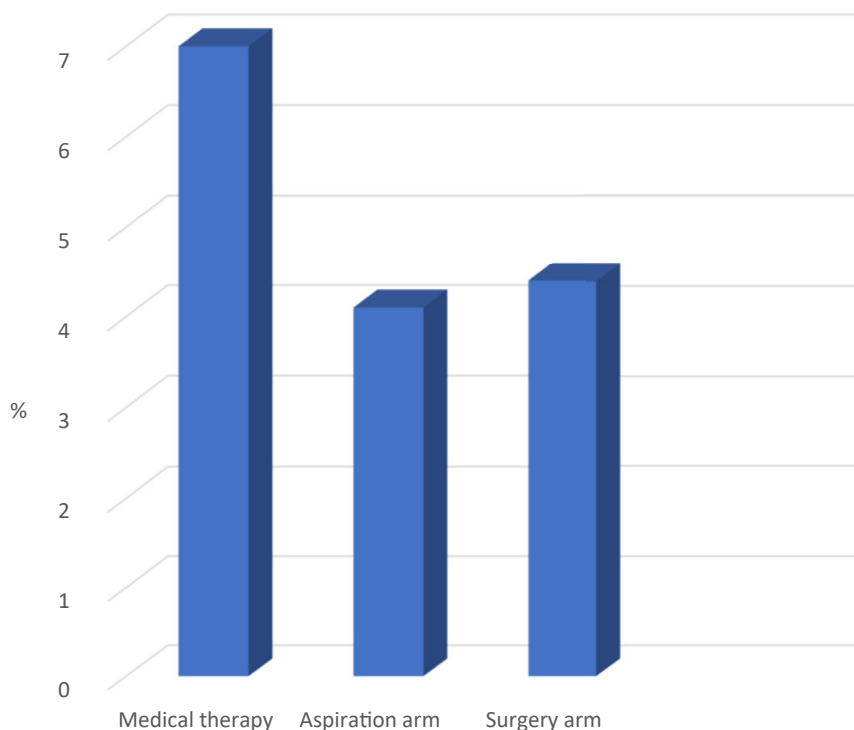


Figure 2. Mortality percentage in each arm.

Table 2. Multivariable logistic regression analysis to predict inpatient mortality in high-risk patients with tricuspid valve infective endocarditis

Variable	OR	95% CI for OR	P
Treatment modality			
Aspiration	1		Ref
Surgery	1.368	0.821–2.280	0.228
Medical treatment	2.963	1.824–4.812	< 0.001
Age, y	1.027	1.022–1.032	< 0.001
Sex			
Male	1		Ref
Female	0.945	0.844–1.058	0.326
Race			
White	1		Ref
Black	0.847	0.698–1.027	0.091
Hispanic	0.964	0.780–1.191	0.734
Other	1.612	1.247–2.084	< 0.001
Primary insurance			
Medicare	1		Ref
Medicaid	1.140	0.944–1.377	0.172
Private insurance	0.971	0.773–1.220	0.800
Other	1.521	1.228–1.885	< 0.001
DM	0.846	0.708–1.012	0.067
CKD	1.400	1.191–1.645	< 0.001
Obesity	0.607	0.488–0.755	< 0.001
CAD	1.056	0.848–1.314	0.628
Smoking	0.743	0.659–0.838	< 0.001
Septic shock	6.680	5.876–7.595	< 0.001
Alcohol	0.882	0.704–1.104	0.272
Acute respiratory failure	7.346	6.357–8.489	< 0.001
Substance abuse	0.607	0.530–0.696	< 0.001
MSSA	0.727	0.633–0.835	< 0.001
MRSA	0.815	0.711–0.935	0.003
Presence of PM and/or ICD	0.483	0.305–0.763	0.002
Acute RV failure	1.271	0.844–1.913	0.251
History of cardiac surgery	1.680	1.284–2.198	< 0.001
History of systolic heart failure	0.821	0.666–1.012	0.064

CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; DM, diabetes mellitus; ICD, implantable cardiac defibrillator; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; OR, odds ratio; PM, pacemaker; Ref, reference; RV, right ventricular.

33 years (range: 28–44) and more than two thirds (73%) of the cohort patients had a history of drug use. Patients treated with percutaneous aspiration had the highest prevalence of septic shock (41.2%, vs 27.9% and 24.8% in the surgical and conservative group, respectively; $P < 0.001$) and acute respiratory failure (37.9%, vs 36.5% and 30.4% in the surgical and conservative group, respectively; $P < 0.001$).

Primary outcome

The overall in-hospital mortality rate was 7% ($n = 2000$). Patients who were treated conservatively had higher in-hospital mortality rates (7.5%), compared to those of the surgical group

(4.4%) and of the percutaneous aspiration group (4.1 %; $P < 0.001$; Fig. 2). In a multivariate analysis, factors associated with increased risk of in-hospital mortality included the following: age (odds ratio [OR] 1.027, 95% confidence interval [CI] 1.022–1.032, $P < 0.001$); chronic kidney disease (OR 1.4, 95% CI 1.191–1.645, $P < 0.001$); septic shock (OR 6.68, 95% CI 5.876–7.595, $P < 0.001$); acute respiratory failure (OR 7.346, 95% CI 6.357–8.489, $P < 0.001$); and medical therapy (OR 2.963, 95% CI 1.824–4.812, $P < 0.001$). The adjusted risk of in-hospital mortality did not differ significantly between the aspiration and surgical groups ($P = 0.228$). The complete multivariable analysis is presented in Table 2.

Secondary outcomes

The disposition of patients varied significantly among the study groups ($P < 0.001$). Patients in the aspiration group had the highest rate of home discharge with self-care (34.3%), compared to that in the surgical group (33.8%) and in the conservative group (28.4%). The median length of stay was the longest in the surgery group (27 days, IQR 17–45), followed by the aspiration group (21.5 days, IQR 13–39), and then the medical treatment group (13 days, IQR 6–25; $P < 0.001$). The median total charges were highest in the surgery group (\$391,581, IQR \$263,575–\$616,512), followed by the aspiration group (\$267,502, IQR \$156,035–\$417,308), and then the medical treatment group (\$109,256, IQR \$50,591–\$216,774; $P < 0.001$). Secondary outcomes are presented in Table 3.

Subgroup analysis

Subgroup analysis of the primary outcome demonstrated that benefit from intervention was observed in patients aged < 65 years (OR 0.48, 95% CI 0.34–0.7), and even greater benefit for those aged < 45 years (OR 0.33, 95% CI 0.26–0.41), whereas conservative therapy was favoured in patients aged ≥ 65 years (OR 2.14, 95% CI 1.26–3.63). The benefit was seen in both female and male patients, and in patients with either a presence or an absence of a history of substance use. In patients with septic shock and those with respiratory failure, an interventional approach yielded a better outcome (OR 0.32, 95% CI 0.26–0.40; OR 0.34, 95% CI 0.28–0.42, respectively), whereas no difference was seen in patients without septic shock or respiratory failure (Fig. 3).

Discussion

In this analysis of a large database—the NIS—we compared the characteristics and in-hospital outcomes of

Table 3. Secondary outcomes, according to treatment group

Secondary outcome	Percutaneous aspiration group	Surgery group	Conservative-therapy group	P
Length of stay, d (IQR)	21.5 (13–39)	27 (17–45)	13 (6–25)	< 0.001
Disposition of patients, n (%)				
Home with self-care	170 (34.3)	1240 (33.8)	6330 (28.4)	< 0.001
Home with home care	60 (12.1)	570 (15.6)	1840 (8.2)	
To another facility	240 (48.5)	1625 (44.3)	9375 (42)	
Discharge AMA	25 (5.1)	230 (6.3)	4770 (21.4)	
Total charges (IQR), \$	267,502 (156,035–417,308)	391,581 (263,575–616,512)	109,256 (50,591–216,774)	< 0.001

AMA, against medical advice; IQR, interquartile range.

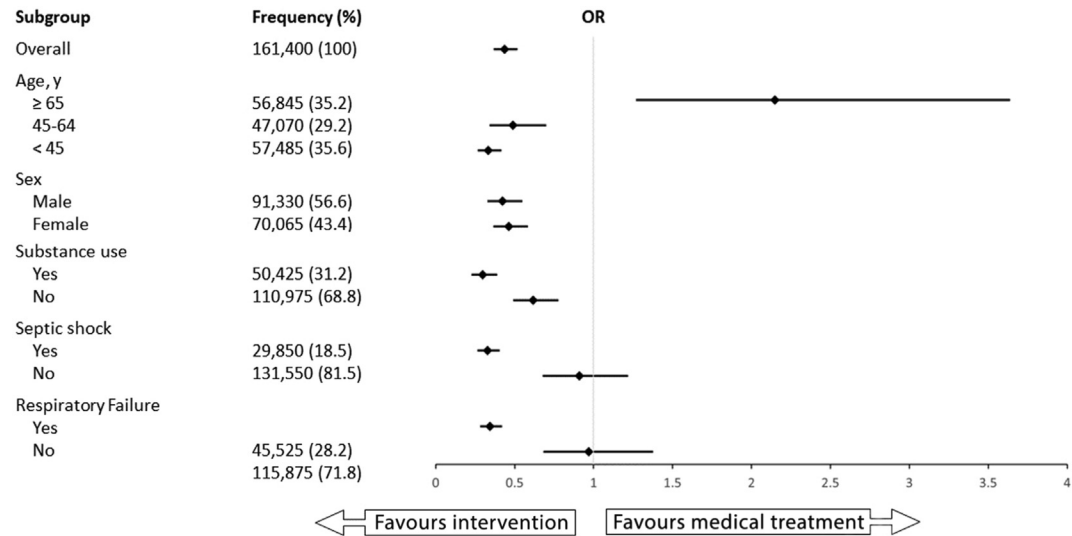


Figure 3. Forest plot of subgroup analysis. OR, odds ratio.

high-risk patients with TV IE treated with percutaneous aspiration vs with either surgical or conservative management. The main finding of this study is that patients undergoing percutaneous aspiration had the lowest mortality rates, despite their being more unstable than those in the other groups. Remarkably, the risk of mortality with conservative treatment was almost 3 times higher than that in patients treated with percutaneous aspiration.

The overall mortality rate for patients with TV IE in the present study is in line with previous data.² However, patients treated with surgery had a lower mortality rate,¹³ perhaps owing to improved surgical techniques, as the analysis included admissions that occurred between 2017 and 2019, as opposed to older available data. Notably, an even lower mortality rate was observed with a percutaneous approach. The risk of mortality with a percutaneous approach was comparable to that with surgery; but given that the approaches have similar outcomes, the less-invasive one is preferable. This preference is especially relevant in a population of a high prevalence of IVDUs, who are at risk of reinfection. Moreover, the surgical approach carried the highest financial burden, and was accompanied by a longer length of hospital stay, compared to those with either percutaneous aspiration or conservative management.

With a surgical approach, the vast majority of the vegetation, or possibly all of it, is removed. Percutaneous aspiration removes most but not necessarily all of the infective tissue. Nevertheless, for nonresponders to medical treatment, merely debulking the vegetation carries potential benefit. Suggested mechanisms include disruption of biofilm, and clearing of thrombi, which could serve as a protective layer for the infection.⁸ Accordingly, most patients who undergo percutaneous aspiration for IE have clear blood cultures thereafter.¹⁴ Moreover, given that healed IE carries a lower operative risk of mortality than active IE,¹⁵ even if surgery is indicated for severe tricuspid regurgitation, an initial percutaneous approach may lead to better surgical results. Therefore, the benefits of percutaneous aspiration extend beyond the prevention of emboli.

This study has several limitations that must be considered. First, the rate of hospital discharge against medical

advice was highest in the conservative-therapy group. Although this finding is expected, it introduces selection bias toward better in-hospital outcomes among the conservative group. Additionally, we assumed that all patients who underwent TV aspiration had an indication for surgery, which contributed further to the selection bias. Second, we used ICD codes to identify patients, and the accuracy of doing so is not irrefutable. Nevertheless, ICD codes have been shown to have high specificity and sensitivity, specifically with IE.¹⁶ Third, our study did not include those with a history of recurrent TV IE, and it did not specify the type of surgery patients underwent. Finally, the NIS inpatient data come with limitations in extracting all the relevant data; thus, insights regarding long-term outcomes cannot be drawn from the current results.

Conclusion

Among high-risk patients with TV IE, an invasive approach is associated with a significantly lower in-hospital mortality rate, compared to that with a conservative approach, particularly in younger, unstable patients. Given that percutaneous aspiration is less invasive than tricuspid surgery, and is associated with a lower financial burden, this approach should be considered for first-line therapy, when feasible, in high-risk patients with TV IE.

Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article, as the NIS contains deidentified public data.

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Disclosures

Z.R. is a consultant for Angiodynamics. All the other authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjopen.ca/> and at <https://doi.org/10.1016/j.cjco.2024.05.010>.