Association between the timing of surgery for complicated, left-sided infective endocarditis and survival

Andrew Wang, MD,[a] Vivian H. Chu, MD, MHS,[a] Eugene Athan, MD,[b] Francois Delahaye, MD,[c] Tomas Freiberger, MD, PhD,[d] Cristiane Lamas, MD, MRCP, PhD,[e] Jose M. Miro, MD, PhD,[f] Jacob Strahilevitz, MD,[g] Christophe Tribouilloy, MD, PhD,[h] Emanuele Durante-Mangoni, MD, PhD,[i] Juan M. Pericas, MD, PhD,[f] Nuria Fernández-Hidalgo, MD, PhD,[j] Francisco Nacinovich, MD,[k] Bruno Barsic, MD,[l] Efthymia Giannitsioti, MD,[m] John P. Hurley, MD, FRCSI,[n] Margaret M. Hannan, MD,[n] and Lawrence P. Park, PhD[a], for the ICE-PLUS Investigators
Durham, NC; Geelong, Australia; Lyon-Bron, Amiens, France; Brno, Czech Republic; Rio de Janeiro, Brazil; Barcelona, Spain; Jerusalem, Israel; Naples, Italy; Buenos Aires, Argentina; Zagreb, Croatia; Athens, Greece; Dublin, Ireland

Background In patients with active infective endocarditis (IE), the relationship between timing of surgery and survival is uncertain. The objective was to evaluate clinical characteristics associated with timing of surgery and the association between surgical timing and 6-month survival in complicated, left-sided IE.

Methods In a prospective, multicenter, observational registry (The International Collaboration on Endocarditis-PLUS, registry from 2008 to 2012), clinical factors associated with timing of surgery during the index hospitalization were determined among 485 adult patients with definite, complicated, left-sided IE who underwent cardiac surgery during their index hospitalization. The relationship between early surgical intervention (<7 days from admission to surgery center) and outcome after surgery was analyzed. The primary end point of the study was 6-month survival.

Results The median time to surgery from admission to surgical center was 7 (interquartile range 2-15) days. Patients who underwent earlier surgery were more likely transferred to the surgical center (74.2% vs 46.4%, *P* < .001) and had a lower percentage of preexisting heart failure (before IE diagnosis) (6.0% vs 17.3%, P < .001) but higher rate of acute heart failure (53.2% vs 38.4%, *P* = .001). Variables independently associated with surgery <7 days from admission were patient transfer, acute heart failure, and nonelective surgical status (*C*-index = 0.84), but predicted operative risk was not. Cox proportional hazards modeling with inverse probability of treatment weighting found that earlier surgery was associated with a trend toward higher 6-month mortality compared with later surgery (hazard ratio = 1.68, 95% CI 0.97-2.96; *P* = .065), particularly surgery within 2 days of admission or transfer. Mortality was significantly associated with operative risk and complicated IE, including *Staphylococcus aureus* infection and presence of abscess.

Conclusions Earlier surgery in IE is strongly associated with acute heart failure and surgical urgency. After adjustment for operative risk and IE complications, earlier surgery <7 days from admission was associated with a trend toward higher 6-month overall mortality compared with surgery later in the index hospitalization. (Am Heart J 2019;210:108-116.)

Surgery for left-sided infective endocarditis (IE) is indicated and recommended in cases of IE complicated by acute heart failure, abscess or fistula formation, persistent bacteremia, recurrent embolic events, or large vegetation.[1-3] Approximately one-half of patients with IE undergo surgery during their index hospitalization for IE before the completion of antibiotic therapy,[4] and surgery has been associated with survival benefit in patients with

From the [a]Duke University Medical Center, Durham, NC, [b]Barwon Health and Deakin University, Geelong, Australia, [c]Hospital Louis Pradel, Lyon-, Bron, France, [d]Centre for Cardiovascular Surgery and Transplantation, Brno, and Central European Institute of Technology, Masaryk University, Brno, Czech Republic, [e]Instituto Nacional de Cardiologia and Unigranrio, Rio de Janeiro, Brazil, [f]Infectious Diseases Service, Hospital Clinic–IDIBAPS, University of Barcelona, Barcelona, Spain, [g]Hadassah-Hebrew University Medical Center, Jerusalem, Israel, [h]University Hospital, Amiens, France and INSERM U-1088, University of Picardie, Amiens, France, [i]Internal Medicine, University of Campania, Monaldi Hospital, Naples, Italy, [j]Servei de Malalties Infeccioses, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain, [k]Instituto Cardiovascular de Buenos Aires, Buenos Aires, Argentina, [l]School of Medicine University of Zagreb, Hospital for Infectious Diseases, Zagreb, Croatia, [m]Attikon University General Hospital, Athens, Greece, and [n]Mater Misericordiae University Hospital, Dublin, Ireland.

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Reprint requests: Andrew Wang, MD, DUMC 3428, Duke Hospital, Room 7401, 2301 Erwin Rd, Durham, NC 27710.
E-mail: a.wang@duke.edu

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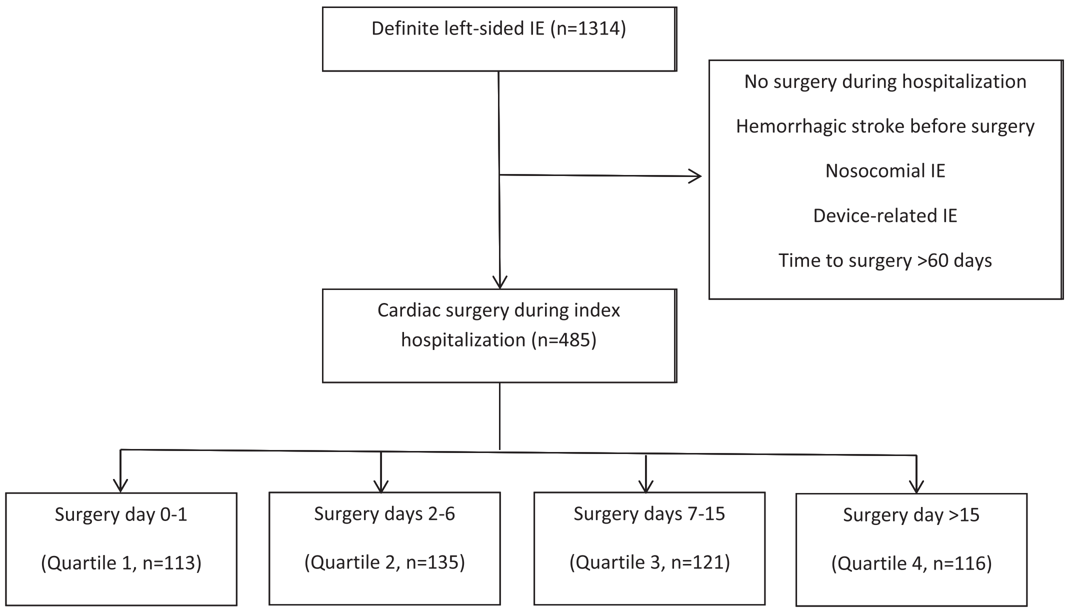
Figure 1



Study population from ICE-PLUS registry.

complicated IE.[5,6] However, the appropriate timing of surgery in IE for optimal outcome is not clearly defined.[7]

Earlier surgery in IE has been found to reduce systemic embolic events without difference in mortality in the randomized EASE trial, in which surgery occurred within 48 hours of randomization.[8] In contrast, a recent American Heart Association scientific statement defined *early surgery* as surgery performed during index hospitalization and before completion of a full course of antibiotics.[1] This broad span of time for surgery during the index hospitalization may be highly variable[4] and typically delayed in comparison with the EASE trial protocol. In contrast, European guidelines differentiate surgical timing as emergent (performed within 24 hours), urgent (within a few days), or elective surgery (after 1 to 2 weeks of antibiotic therapy) after surgical indication, with surgery advised on an urgent basis for the majority of cases.[3]

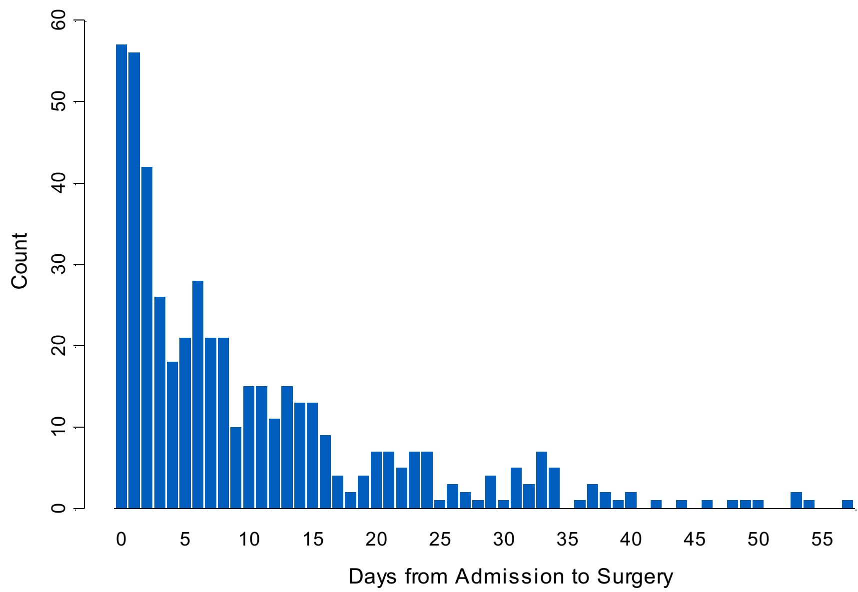
A recent meta-analysis of 21 observational studies of surgical treatment of IE found that surgery performed at 7 days or less from admission had the lowest risk of all-cause mortality but without adjustment for operative indication, risk, or urgency.[9] Given the uncertain influence of surgical timing on outcome in IE, we hypothesized that patients with IE undergoing earlier surgery, after adjustment for clinical factors related to surgical timing, have improved survival compared with later surgery during the index hospitalization. The objectives of this study were (1) to evaluate clinical factors associated with timing of surgery in left-sided IE during the index hospitalization and (2) to evaluate the relationship between surgical timing and in-hospital IE complications and 6-month survival after surgery.

Methods

The study population for this analysis was the International Collaboration on Endocarditis (ICE)-PLUS cohort, a prospective, multinational registry of consecutive cases of definite IE by modified Duke criteria,[10] with prespecified definitions of variables, as previously described.[6,11] The ICE-PLUS registry includes 2,124 IE patients from 34 centers in 18 countries hospitalized between September 1, 2008, and December 31, 2012, with 6-month vital status follow-up data (all ICE sites listed in Appendix).

Patients with definite, left-sided IE according to modified Duke criteria who underwent cardiac surgery during the index hospitalization were included in the study. Cases of device-related IE were excluded from the analysis. In addition, to reduce confounding related to surgical timing, other exclusion criteria were hemorrhagic stroke before surgery, nosocomial IE, and surgery performance >60 days from admission. To preserve the assumption of independence of observations, only the first episode of IE recorded for an individual patient was used. The study cohort is shown in Figure 1. The study was approved by the institutional review board or ethics committee at all participating sites, according to local standards.

Figure 2



Histogram of surgical timing during index hospitalization for IE.

Definitions

Definitions of the standard variables used in the ICE-PLUS database have been reported previously.[4,6,11] The index hospitalization was defined as time between date of admission or transfer to ICE hospital to the date of discharge. Surgery during this hospitalization was defined by investigators at participating hospital as *elective*: the patient's cardiac function has been stable in the days or weeks prior to the operation, and the procedure could be deferred without increased risk of compromised cardiac outcome; *urgent*: surgical procedure is required during the same hospitalization to minimize chance of further clinical deterioration; or *emergent*: patient is having ongoing, refractory (difficult, complicated, and/or unmanageable) unrelenting cardiac compromise, with or without hemodynamic instability, and not responsive to any form of therapy except cardiac surgery.[12] The risk scoring system based on the Surgical Thoracic Society (STS) Adult Cardiac Surgery Database (STS-IE score) was used to calculate predicted risk of operative mortality for the study cohort.[12] All IE complications were events before the date of surgery. *Large vegetation* was defined as maximum diameter >10 mm by echocardiography.

Descriptive statistics

Baseline characteristics and clinical events of the quartiles of surgical timing are presented as medians with 25% and 75% percentile for continuous variables and frequencies with proportions for categorical variables. Statistical comparisons between groups were made with Wilcoxon rank-sum test for continuous variables and Fisher exact test for categorical variables.

Propensity score model

A multivariable logistic regression model was fit to calculate a propensity score (probability) for early surgical treatment. The response variable was receipt of cardiac surgery for IE during the index hospitalization at time less than median time to surgery. The model included variables that were selected a priori by an experienced cardiologist (A. W.) and from practice guidelines[2,3] and previous studies[4,13,14] as those that would be evaluated in the decision to treat IE with surgery. These variables were age, history of cardiac surgery, history of atrial fibrillation, history of heart failure, history of injection drug use, transfer, prosthetic valve IE, new moderate/severe aortic regurgitation, *Staphylococcus aureus* IE, enterococcus IE, acute heart failure, embolism before surgery, abscess, vegetation size/mobility, and resistant microorganism. The predicted probabilities of surgery were calculated and used as inverse probability weights in predicting outcome. Weights were trimmed at 20 to avoid overly influential observations.

Survival analysis

A Cox proportional hazards model to predict survival at 6 months after discharge was fit in the ICE-PLUS data set, including variables associated with survival at

Table I. Quartiles of timing of cardiac surgery for IE (n = 485) in the ICE-PLUS registry, 2008-2012

Variable	Quartile 1 n = 113	Quartile 2 n = 135	Quartile 3 n = 121	Quartile 4 n = 116	*P* value
Median age, IQR	54.6 (40.8-66.0)	55.6 (40.7-66.6)	56.6 (41.5-69.5)	60.6 (46.7-70.5)	.12
Male sex	78 (69)	103 (76.3)	89 (74.2)	80 (69)	.47
History of atrial fibrillation	10 (9.2)	9 (6.9)	17 (14.8)	12 (11.4)	.23
History of heart failure	6 (5.5)	9 (6.7)	21 (17.5)	20 (17.5)	.002
Diabetes mellitus	11 (10.2)	23 (17.2)	21 (17.5)	19 (16.5)	.36
Renal disease	6 (5.4)	6 (4.5)	9 (7.4)	9 (7.9)	.66
Dialysis	1 (0.9)	3 (2.2)	2 (1.7)	4 (3.4)	.61
HIV	4 (3.7)	1 (0.8)	0	0	.022
Injection drug use	11 (9.7)	6 (4.5)	6 (5)	2 (1.7)	.062
Immunosuppression	4 (3.6)	3 (2.2)	2 (1.7)	8 (7)	.15
Liver disease	4 (3.6)	2 (1.5)	3 (2.5)	3 (2.6)	.75
History of cancer	9 (8.1)	12 (9)	8 (6.7)	13 (11.4)	.65
Transfer	97 (86.6)	87 (64.9)	62 (51.2)	48 (42.1)	<.001
Prosthetic valve IE	12 (10.6)	19 (14.1)	24 (19.8)	29 (25)	.020
Microbiology					
S aureus	20 (17.7)	25 (18.5)	13 (10.7)	15 (12.9)	.25
Coagulase-negative *Staphylococcus*	5 (4.4)	9 (6.7)	7 (5.8)	6 (5.2)	.92
Viridans streptococci	17 (15)	31 (23)	20 (16.5)	34 (29.3)	.032
Enterococcus	14 (12.4)	10 (7.4)	19 (15.7)	11 (9.5)	.18
Culture negative	18 (16.2)	23 (17.3)	20 (16.8)	19 (16.8)	>.99
Echocardiographic findings					
Vegetation	113 (100)	135 (100)	121 (100)	116 (100)	>.99
New mitral regurgitation	58 (53.7)	63 (50)	61 (51.7)	52 (47.7)	.83
New aortic regurgitation	61 (56.5)	61 (48.8)	48 (41)	47 (42.7)	.089
Leaflet perforation	19 (17.1)	35 (25.9)	25 (20.8)	25 (21.7)	.42
Abscess	27 (25.5)	34 (26.4)	30 (26.3)	25 (23.6)	.96
Fistula	3 (2.7)	6 (4.5)	5 (4.2)	1 (0.9)	.33
IE complications before surgery					
Acute heart failure	65 (60.2)	67 (54)	51 (45.1)	40 (37.4)	.004
New NYHA 3 or 4 heart failure	30 (36.6)	47 (43.1)	32 (29.1)	30 (27.8)	.065
Stroke	16 (14.2)	18 (13.3)	15 (12.5)	22 (19.3)	.47
Abscess	29 (29)	41 (34.2)	34 (31.2)	27 (25.5)	.55
Emboli	39 (36.4)	35 (28.2)	32 (28.8)	25 (22.7)	.17
Persistent bacteremia	6 (5.6)	11 (9.1)	6 (5.6)	10 (9.8)	.51
Outcome					
In-hospital mortality	15 (13.4)	19 (14.1)	13 (10.8)	16 (13.8)	.87
6-m mortality	17 (15.2)	24 (17.8)	16 (13.3)	17 (14.7)	.80

Quartile 1 = day 0-1, quartile 2 = day 2-6, quartile 3 = day 7-15, and quartile 4= >day 15. *NYHA*, New York Heart Association.

$P < .15$ in univariable analysis. Two models were fit. In the first, surgery was included as an indicator variable for surgery performed <7 days after admission, with weighting by the inverse probability (propensity) of early surgery. To explore the timing of surgery in more depth, a second model (without inverse probability weighting) included day of surgery since admission or transfer as individual indicator variables for days 0, 1, 2, 3, 4-5, and 6-7, with surgery on days 8 and later as the reference level. Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC), and plots were generated with Splus 8.1 (TIBCO Software Inc, Palo Alto, CA).

Results

The median time to surgery was 7 days (interquartile range [IQR] 2-15), and the time to surgery relative to admission to ICE surgical center is shown in Figure 2. The clinical, microbiologic, and echocardiographic characteristics of the patients who met study inclusion criteria and underwent surgery during index hospitalization for IE (n = 485) in the ICE-PLUS registry are shown in Table I by quartile of surgical timing (quartile 1 = 0-1 day, quartile 2 = 2-6 days, quartile 3 = 7-15 days, quartile 4= >15 days). Patients who underwent earlier surgery had a lower percentage of preexisting heart failure (before IE diagnosis) but a higher rate of acute heart failure.

Two hundred ninety-four patients (61%) were transferred from another hospital to a surgical center, and the proportion of patients who had been transferred from other facilities was higher among earlier surgical groups. The median time from other hospital admission to transfer date was 8 (IQR 4-19) days. Patients transferred to a surgical center in ICE-PLUS were more likely to have

Table II. Indications for surgery and operative risk across quartiles of surgical timing

Indication	Quartile 1 n = 113	Quartile 2 n = 135	Quartile 3 n = 121	Quartile 4 n = 116	*P* value
Heart failure	35 (31)	60 (44.4)	42 (34.7)	43 (37.1)	.16
Embolism	28 (24.8)	34 (25.2)	26 (21.5)	21 (18.1)	.52
Abscess	21 (18.6)	27 (20)	30 (24.8)	17 (14.7)	.27
Valvular regurgitation	70 (61.9)	90 (66.7)	79 (65.3)	74 (63.8)	.88
Large vegetation	75 (66.4)	75 (55.6)	52 (43)	53 (45.7)	.001
Resistant organism	8 (7.1)	17 (12.6)	9 (7.4)	7 (6)	.28
STS-IE score	22 (15-32)	22 (16-37)	22 (15-32)	22 (10-31)	.33
Surgery status					
Elective	7 (6.7)	17 (13.1)	48 (41.4)	68 (58.6)	<.001
Urgent	78 (74.3)	99 (76.2)	63 (54.3)	40 (34.5)	
Emergent	20 (19)	14 (10.8)	5 (4.3)	8 (6.9)	

S aureus infection, new mitral valve regurgitation, and large vegetation yet had similar operative risk score (Supplemental Table I).

The indications for surgical intervention as determined by the local IE team are shown in Table II. The difference between date of admission versus date of surgical indication was 1.1 (IQR 0-3) days. These indications were similar across the time intervals of surgery, although patients who had earlier surgery were more likely to have a large vegetation, but there was no difference in embolic events. There was no difference in operative risk by STS-IE score across the time intervals, but earlier surgery was strongly associated with urgent or emergent status. In multivariable analysis (Supplemental Table II), patient transfer, acute heart failure, and surgical urgency or emergency were strongly associated with surgery <7 days from admission; prior history of heart failure before IE was associated with later surgery (model *C*-index = 0.84).

Unadjusted analysis showed no significant difference in 6-month survival across the quartiles of surgical timing. Cox proportional hazards modeling with propensity adjustment for surgical timing identified host (sex, diabetes mellitus, prior IE, kidney disease, and operative risk), microbiologic (*S aureus* IE), and IE complication (abscess) variables and transfer status to be independently associated with 6-month mortality (Table III). Earlier surgery <7 days from admission was associated with a trend toward higher 6-month mortality compared with later surgery (hazard ratio [HR] = 1.68, 95% CI 0.97-2.96; *P* = .065) (Figure 3). Unadjusted survival analysis based on timing of surgery and transfer status also showed similar survival rates (Supplemental Figure 1). In analyzing the timing of surgery by day, the risk of 6-month mortality was highest for patients who underwent surgery within the initial 2 days after admission or transfer (Figure 4 and Supplemental Table III).

Because a strong association between acute heart failure and earlier surgery was found, we evaluated the relationship between timing of surgery for this indication and outcome (Table IV). Patients with acute heart failure who had earlier surgery had a higher operative risk by STS-IE score but no difference in in-hospital or 6-month mortality after discharge. The HRs and 95% CI for early surgery for other IE complications are shown in Table V. Early surgery was not associated with lower 6-month mortality for any surgical indication but was associated with higher 6-month mortality for patients with abscess (HR 2.09, 95% CI 1.31-3.34) or prosthetic valve infection (HR 5.36, 95% CI 2.81-9.53).

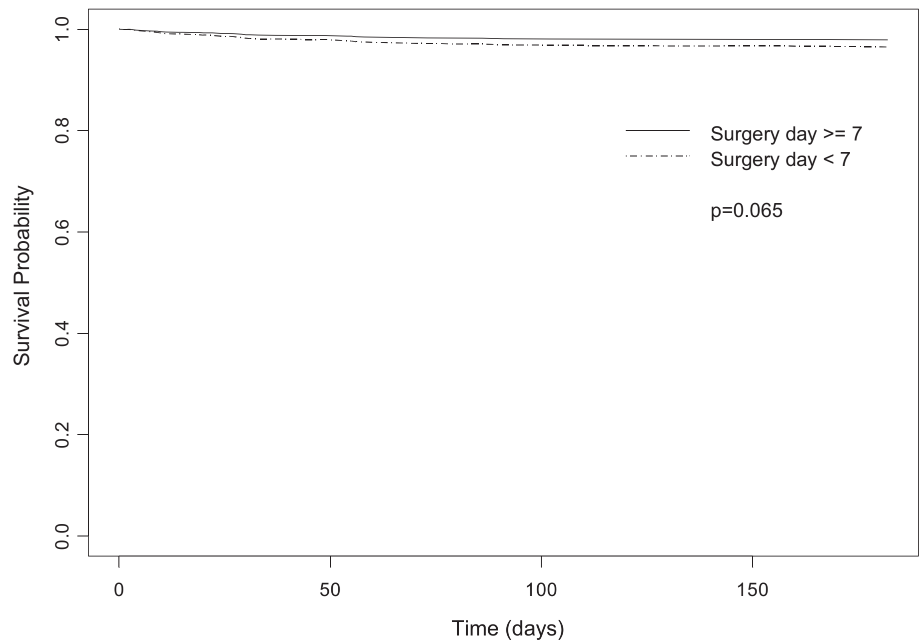
Table III. Clinical variables independently associated with 6-month IE mortality in Cox proportional hazards model

Variable	Hazard ratio (95% CI)
Surgery <7 d from admission	1.68 (0.97-2.96)
Age, y	
45-60	0.39 (0.15-0.94)
61-70	0.58 (0.23-1.33)
>70	1.49 (0.79-2.87)
Male sex	0.35 (0.20-0.62)
Diabetes mellitus	1.95 (1.03-3.60)
Prior kidney disease	4.34 (2.13-8.66)
Transfer	0.52 (0.30-0.89)
Previous IE	3.49 (1.58-7.34)
S aureus IE	2.28 (1.19-4.26)
Abscess	2.26 (1.24-4.08)
STS-IE score	
Quartile 2 (14-21)	6.54 (1.81-35.30)
Quartile 3 (21-32)	6.21 (1.79-32.82)
Quartile 4 (32-74)	6.89 (2.00-36.34)

Discussion

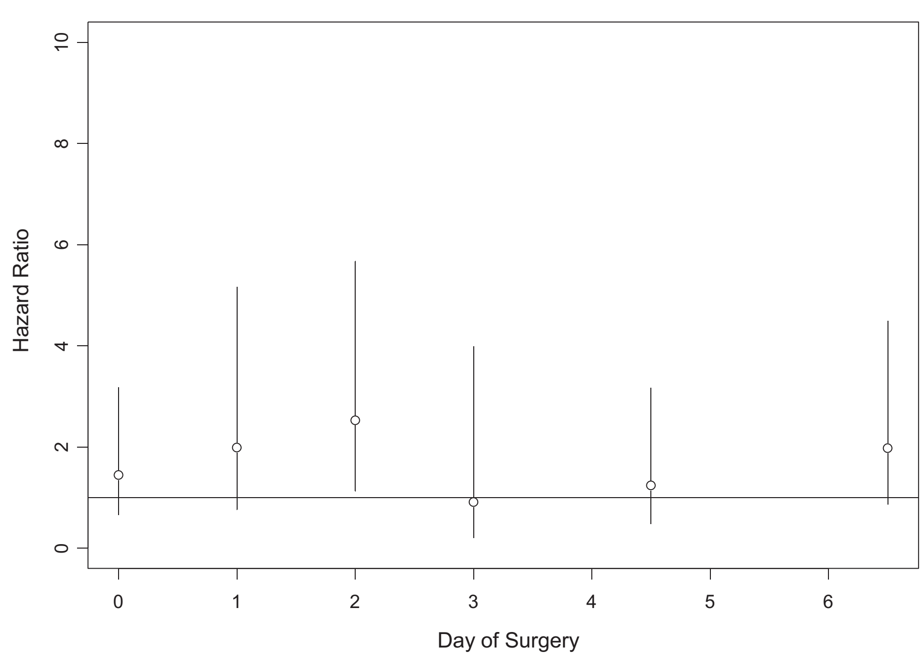
A high percentage of patients with left-sided IE develop indications for surgical intervention, generally soon after IE diagnosis,[4] but the relationship between surgical timing and outcome is not well defined. In this prospective, multinational cohort of IE, we found that earlier surgery <7 days from admission is strongly predicted by acute heart failure, referral, and surgical

Figure 3



Predicted survival rates from Cox proportional hazards model for early versus delayed surgical intervention in complicated, left-sided IE. Survival probabilities were calculated for patients with no risk factors among the variables included in the model (eg, youngest age category, no heart failure).

Figure 4



Cox proportional hazard ratios for 6-month mortality based on day of surgical intervention in complicated, left-sided IE. Point estimates and 95% CI are shown for surgery on days 0, 1, 2, 3, 4-5, and 6-7. The horizontal line is the reference category surgery on days 8 and later.

Table IV. Operative risk and outcome in IE patients with acute heart failure based on timing of surgery

	Quartile 1 n = 70	Quartile 2 n = 80	Quartile 3 n = 62	Quartile 4 n = 53	*P* value
STS-IE score	24 (16-37)	28.0 (19-49)	23 (16-33)	25 (19-39)	.026
In-hospital mortality	9 (12.9)	14 (17.5)	6 (9.8)	9 (17.0)	.55
6-m mortality	11 (15.7)	16 (20)	6 (9.8)	9 (17.0)	.43

Table V. Adjusted risk of 6-month mortality after earlier surgery for specific IE complications

IE complication	HR (95% CI)
Acute heart failure (n = 223)	0.90 (0.57-1.40)
Embolic event (n = 131)	0.70 (0.40-1.16)
Abscess (n = 131)	2.09 (1.31-3.34)
Stroke (n = 71)	0.74 (0.34-1.42)
Persistent bacteremia (n = 33)	1.91 (0.82-3.85)
Prosthetic valve IE (n = 84)	5.36 (2.81-9.53)

urgency but not other surgical indications. A high percentage of patients with surgical indications undergo surgery within the first week of admission, and early surgery <7 days from admission to a surgical center was not associated with lower overall 6-month mortality but rather a trend toward higher mortality compared with later surgery after propensity adjustment.

Early surgery has been broadly defined as surgery at any time during the index hospitalization for IE[1] and has been associated with lower mortality in patients with complicated IE.[5,6,15,16] However, IE complications typically occur early in the course of treatment,[17,18] and the duration of hospitalization for IE may be several weeks, thus offering a long time interval to perform surgery. In the only randomized study of surgical timing in IE in 76 patients, surgery performed within 2 days of randomization resulted in a lower rate of systemic embolic events but no difference in 6-month mortality.[8] Notably, prespecified surgical indications in that trial were the presence of a large vegetation and severe valvular regurgitation, but the study excluded patients with other standard surgical indications, such as moderate-to-severe heart failure, abscess, or heart block.[8] In addition, patients were young persons with mostly streptococcal IE, which may be a more favorable patient profile for very early surgery and not representative of IE in larger, multicenter studies.[13] In contrast to the EASE trial,[8] the present study involved a larger, more generalizable cohort of IE with standard and diverse surgical indications.

Other retrospective, observational studies of surgery in IE have been limited by lack of data and adjustment for important surgical considerations such as indication, timing of indication, and operative risk.[9] A previous retrospective study of 291 IE patients in France found that surgery ≤7 days was associated with similar 6-month survival as later surgery, but did not adjust for survival bias or operative risk.[19] Because patients with higher operative risk due to comorbid conditions may have no or delayed surgical intervention, observational studies may be biased by selection of lower-risk patients for earlier surgery. Our results confirm that early surgery, after propensity adjustment for clinical characteristics including indication and operative risk, was associated with similar overall mortality at 6 months.

In the setting of left-sided IE, acute heart failure is a common, often poorly tolerated complication with a high mortality if untreated[18] and is the most common indication for surgery in IE. Given the lack of medical therapies for acute valvular regurgitation and heart failure, it is not surprising that this IE complication was the strongest predictor of early surgery. However, earlier surgery in patients with acute heart failure was not statistically associated with lower mortality at 6 months. Although surgery for acute heart failure may be required and performed as soon as possible, the risk of operative mortality and morbidity is increased in such urgent situations.[12] Even when heart failure symptoms occur in IE, medical therapy may improve clinical status in some patients[20] such that the urgency of surgery is temporized though still required.

Whereas surgery may be performed as soon as possible for any IE complication, the present study suggests that the association between timing of surgery and outcome may be influenced by the specific surgical indication or other clinical factors. Delaying surgical intervention after an IE complication may be clinically warranted for additional diagnostic testing, to stabilize the patient's condition, or to treat comorbid conditions. For example, in IE complicated by major cerebrovascular event, such as hemorrhagic stroke or infarction with significant neurologic impairment, delay in surgery is recommended to reduce postoperative worsening of neurologic function.[21,22] Our study did not identify any specific surgery indication in IE for which earlier surgery was associated with lower overall mortality.

When other surgical indications occur in active IE, the urgency of surgical intervention may be lower, and the clinical benefit of surgery soon after the diagnosis of IE may be less evident. Surgery was also performed earlier in patients with large vegetation, likely to reduce the risk of embolic event. However, >40% of patients with large vegetation underwent delayed surgery without a higher rate of in-hospital embolic events in our study, which is consistent with previous data suggesting that the risk of embolic events diminishes after the first week of appropriate antibiotic therapy.[17] In prosthetic valve IE, we previously found that surgery during the index hospitalization improved 1-year overall survival only for those patients with additional complications such as significant valvular regurgitation or dehiscence.[5] Delaying surgery after an indication has occurred may be appropriate to assess operative risk and long-term prognosis in patients with such complications before proceeding with surgery.[4] Indeed, operative risk as assessed by STS-IE score was the strongest predictor of 6-month mortality in the present study, although predicted mortality did not differ between patients who had earlier versus delayed surgery.

An observational analysis of the large STS database found that surgery during the active treatment of IE with antibiotics was associated with a significantly higher risk of in-hospital or operative mortality than surgery after the completion of antibiotic therapy.[12] Our observed trend toward lower mortality in patients with delayed surgery (7 or more days) supports that surgical urgency is strongly associated with higher mortality and raises the question of whether early medical interventions, including but not limited to antibiotic therapy, may ameliorate some adverse clinical characteristics in complicated IE without increasing mortality. However, as shown by the survival model with propensity adjustment for early surgery, adverse host factors and IE characteristics are more strongly associated with survival than the timing of surgery. The use of multidisciplinary care teams for IE patients[1,23] treated at the ICE sites may optimize both the use and timing of surgery, as recommended by recent guidelines.[1,3] Multidisciplinary care of IE has been associated with higher use of surgery,[24] but the relationship with surgical timing is unknown.

Patients transferred to a participating ICE hospital with surgical capabilities had differences in IE characteristics (more prosthetic valve IE, *S aureus* infection, large vegetation, and severe valvular regurgitation) and higher surgical urgency but similar comorbid conditions compared with nontransferred patients. These difference among transferred patients demonstrate a selection bias in identifying IE patients with serious complication who were likely to benefit from surgical intervention, but also an inherent delay from time of IE diagnosis to surgical consideration. After adjustment for these adverse clinical characteristics and variables related to earlier surgery, transferred patients were found to have lower 6-month mortality. In previous studies, referral bias was not found to be associated with in-hospital mortality.[25,26] These differing results are likely related to the focus solely on patients treated with surgery and a longer survival end point in the present study.

Although this study had advantages of prospective data collection across different geographic regions, validated assessment of operative risk, and follow-up beyond the operative period, there are several limitations. All participating ICE sites are referral centers with multidisciplinary experience in the management of IE and the availability of cardiac surgery, which may affect the generalizability of the results. The use or timing of surgery was not prespecified by a study protocol but rather was at the discretion of the treating care teams. However, we have previously found that surgery was performed for guideline-directed indications[1-3] in this cohort.[4] There was inherent selection bias in the referral of patients to an ICE-PLUS site and in the use and timing of surgery, although adjustment for transfer status was performed. The time from admission to transfer was not evaluated in the analyses because of incomplete clinical data prior to treatment at an enrolling ICE center. As an observational study, other clinical variables not collected or included in the models may be associated with timing of surgery or mortality, or may confound the relationships between defined variables and outcome. The complexities of surgical indication, risk, selection, timing, and the likelihood of residual confounding factors limit confidence about the effect (both direction and magnitude) of surgery timing on outcome.

In conclusion, the timing of surgery in IE is strongly associated with new-onset or acute heart failure and surgical urgency. Surgery <7 days from admission to a surgical center, particularly urgent surgery within the initial 2 days, was not associated with lower 6-month overall mortality compared with surgery later in the index hospitalization. Although surgery in the few days after IE diagnosis may be clinically indicated for acute heart failure or to reduce the risk of embolic event in the presence of a large vegetation, the routine use of very early surgery for any indication is not supported by current data. Additional studies with attention to specific indication and operative risk are needed to evaluate the influence of surgical timing on survival and other clinical end points in IE.

Disclosures

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Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2019.01.004.

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