Acute Myocardial Ischemia in Patients Receiving Surgery for Acute Type A Aortic Dissection

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Abstract

Purpose: Acute type A aortic dissection (ATAAD) is a dissection involving the ascending aorta within 14 days of symptom onset. Acute myocardial ischemia is associated with short-term mortality in patients with ATAAD. However, its relevance to ATAAD's surgical timing and prognostic implications is unknown. **Methods:** This retrospective study enrolled 277 patients at our tertiary center between March 1997 and January 2019 and investigated their admission electrocardiograms. Twenty-one patients with left ventricular hypertrophy or left bundle branch block were excluded, and the records of 256 patients eventually underwent data collection, review, and multivariate analysis. **Results:** In patients with acute myocardial ischemia, the incidence of aortic root involvement, acute coronary involvement, and preoperative stroke was significantly higher. Acute myocardial ischemia was unassociated with 30-day or in-hospital mortality in patients who underwent surgery within 7 h of symptom onset. However, it was independently associated with the 30-day mortality and postoperative stroke when the 7-hour window had elapsed. **Conclusions:** As a time-dependent surgical prognosticator in ATAAD, acute myocardial ischemia was unassociated with short-term mortality in patients surgically operated within 7 h of symptom onset. Conversely, it was an independent factor for the 30-day mortality and postoperative stroke when the 7-hour window had elapsed.

INTRODUCTION

The clinical features of acute type A aortic dissection (ATAAD) vary and may be nonspecific, often resulting in inaccurate or delayed diagnosis [1, 2]. The acute coronary syndrome (ACS) occurrence considerably outnumbers that of aortic dissections; therefore, initial presentation with symptoms such as acute chest pain may lead to more focus being placed on ACS instead of ATAAD [3]. In addition, misdiagnosis as ACS and the tendency of delayed ATAAD recognition is markedly amplified if ischemic electrocardiogram (ECG) abnormalities are discovered [1, 4-7], particularly in patients simultaneously presenting with chest pain and positive troponin test. Approximately 20–70% of patients with ATAAD have ischemic ECG patterns on admission [4, 6, 8-19], in addition to high complication and short-term mortality rates [8-13, 16-19]. Misdiagnosing ATAAD as ACS results in these patients being erroneously administered antiplatelet or thrombolytic therapy or invasive angiography [12, 20-22], inevitably delaying the urgent ATAAD surgery [1, 2, 20]. Subsequently, such patients may be more likely to experience intraoperative complications such as major bleeding or aortic wall rupture [12].

Previous studies have acknowledged acute myocardial ischemia as an adverse prognosticator of ATAAD; however, there is a high degree of heterogeneity in several ischemia-related variables through which different

ECG criteria were adopted [12, 16, 18]. Furthermore, the association of the timing of surgery with the prognostic significance of acute myocardial ischemia is unclear [8].

We sought to determine whether the period between symptom onset and the surgery can be used for risk stratification when examining the outcomes of short-term mortality and postoperative stroke in patients with ATAAD displaying acute myocardial ischemia on ECG using our tertiary medical center experiences and the updated consensus for a universal definition of myocardial ischemia [23] to overcome the limitations noted in previous studies.

MATERIAL AND METHODS

Study Design and Population

The Institutional Review Board of Kaohsiung Medical University Hospital approved and supervised the study (Approval no: KMUHIRB-(II)20200023; approved on March, 3, 2020).

We conducted a retrospective chart review using medical records abstracted from 277 consecutive patients who underwent surgery for ATAAD in our tertiary center between March 1997 and January 2019, including those who had been diagnosed in surrounding hospitals and transferred to our emergency department. Unlike Kosuge et al. and Hirata et al. [14-17], who included patients admitted within 6 or 12 h of symptom onset, we enrolled all the patients with ATAAD regardless of the ECG acquisition time since we were more concerned with exploring the association between the surgical timing of ATAAD and the prognostic implications of ischemic ECG patterns. Furthermore, for more accuracy, we excluded 21 patients with either left ventricular hypertrophy (LVH) or bundle branch block (BBB) due to the considerable interference of both features with interpreting ischemic ECG abnormalities, overlapping their ECG patterns with probably new ischemic ST-changes [24, 25]. Eventually, 256 patients were dichotomized based on the presence of acute myocardial ischemia on ECG. Acute myocardial ischemia was considered if ST elevation (STE), ST depression (STD), or T-wave inversion (TWI) was displayed (Supplemental Methods S1) [23].

We classified patients by the interval from the onset of symptoms to surgery initiation (time to operation) to investigate the association of ATAAD's surgical timing with the prognostic relevance of acute myocardial ischemia. We performed a receiver operating characteristic (ROC) analysis to determine the optimal cut-off values of time to operation regarding the 30-day mortality and postoperative stroke. The time to operation was 7.83 h for the 30-day mortality and postoperative stroke. The areas under the curves were 0.595 and 0.637 for 30-day mortality and postoperative stroke, respectively. Hence, we hypothesized that the postoperative outcomes of patients with ATAAD not presenting acute myocardial ischemia are similar when surgery is initiated within 7.83 h of symptom onset. For simplicity and clinical application, the 7th hour was the cut-off point classifying our patients into two groups; the early (within 7 h) and late (beyond 7 h) treatment groups.

Definitions (Supplemental Methods S1) and Statistical Analysis

Groups were compared for significant differences in preexisting comorbidities, preoperative characteristics, or postoperative adverse events. In the early and late treatment groups, subgroup analyses of postoperative adverse outcomes were conducted between patients with and without ischemic ECG abnormalities. The Chi-Squared test or Fisher's exact test analyzed the categorical variables. After normality tests, continuous variables were analyzed using Student's t -test or Mann–Whitney U test. In our multivariate analysis, we applied backward elimination to identify independent preoperative factors of acute myocardial ischemia, postoperative stroke, 30-day mortality, and in-hospital mortality. We included all the variables listed in the extreme left column of Tables 1 and 2 as covariates in each binary regression model (36 covariates were included in each model). All our models passed the Hosmer-Lemeshow goodness-of-fit test. Variables with P-values ¡ 0.10 were used in the model entry, and those with P -values > 0.05 were excluded. For discharged patients, regular outpatient clinic visits or phone calls were arranged for follow-up. Kaplan–Meier analysis and log-rank test evaluated the long-term survival via GraphPad Prism (version 9.0.2). The other statistical analyses, including ROC, multivariate analysis, and Hosmer-Lemeshow goodness-of-fit test, were performed using SPSS version 20.0 (IBM. Inc., Chicago, IL, USA).

RESULTS

Demographics, Medical History, and Pre-existing Comorbidities

Two hundred and twenty-seven consecutive patients with ATAAD were enrolled in this study, and their ECGs were analyzed on admission. ECG confounders were observed in 21 (7.6%) patients, and LVH, right bundle branch block (RBBB), and left bundle branch block (LBBB) were discovered in 14 (5.1%), 0 (0.0%), and 7 (2.5%) patients, respectively. According to the aforementioned ECG criteria, 88 (34.4%) patients with acute myocardial ischemia were detected among the 256 patients, and STE was observed in 25 (28.4%) patients. Furthermore, STD or TWI were presented in 63 (71.5%) patients. Concerning patient demographics, medical history, and preexisting comorbidities, apart from COPD or asthma (1.1% ischemia, 10.7% no ischemia, P =0.005), no significant differences were observed between patients with and without acute myocardial ischemia (Table 1).

Preoperative Characteristics

In patients with acute myocardial ischemia (Table 2), the incidence of dissection involving aortic root, detected by computed tomography (CT), was significantly higher (50.0% ischemia, 33.3% no ischemia, P=.009), similar to moderate-to-severe aortic regurgitation (51.1% ischemia, 32.1% no ischemia, P=.003). Patients with acute myocardial ischemia were more likely to harbor acute coronary involvement (22.7% ischemia, 6.5% no ischemia, $P < .001$). In addition, multivariate regression model analysis for acute myocardial ischemia (Supplemental Table S1) presented statistical significance for congestive heart failure history (adjusted odds ratio [OR] 0.37, 95% confidence interval [CI] 0.16–0.86, $P = 0.020$), preoperative stroke (adjusted OR 7.64, 95% CI 1.86–31.45,$P = 0.005$), transient ischemic attack (adjusted OR 0.075, 95% CI 0.01–0.97, $P = 0.047$), moderate-to-severe aortic regurgitation (adjusted OR 1.91, 95% CI 1.03–3.53, $P = 0.039$), and acute coronary involvement (adjusted OR 4.04, 95% CI 1.62–10.07, $P = 0.003$). The overall shock prevalence, defined as preoperative systolic blood pressure below 90 mmHg, and cardiac tamponade, were 20.7% and 23.4%, respectively, and no significant difference was observed between the ischemic and non-ischemic groups (Table 2).

Postoperative Adverse Outcome (Supplemental Table S2)

Regarding postoperative complications, patients in the ischemic group had significantly higher rates of cardiac tamponade ($P = .031$) and ischemic limb neuropathy ($P = .025$) than those in the non-ischemic group. In addition, the length of hospital stay was significantly lower in patients in the ischemic group ($P = 0.039$) than in those in the non-ischemic group. However, further analysis using the Kaplan–Meier curve and log-rank test revealed no significant differences between both groups in terms of long-term survival (Figure 1).

The Surgical Time-Dependent Prognostic Relevance of Acute Myocardial Ischemia

In the early treatment group (within 7 h), the frequencies of postoperative adverse events did not significantly differ between the ischemic and non-ischemic groups (Table 3). In the late treatment group (beyond 7 h), patients with acute myocardial ischemia were more likely to experience stroke postoperatively (29.4% ischemia, 8.9% no ischemia, $P = .002$) (Table 3), primarily during the 7th hour to the 14th hour after symptoms emerged (Supplemental Figure S1). These ischemic patients also had significantly higher 30-day mortality rates (25.5% ischemia, 11.1% no ischemia,P =.007) (Table 3), particularly in those whose time to surgery was between 7 h and 21 h (Supplemental Figure S2). Additionally, in-hospital mortality significantly increased in ischemic patients whose time to surgery was between 14 h and 21 h (Supplemental Figure S3). Despite not including the candidate variable in the model for in-hospital mortality, in two other multivariate regression models, acute myocardial ischemia was an independent factor of the 30-day mortality (adjusted OR 3.30, 95% CI 1.24–8.69, $P = 0.017$) and postoperative stroke (adjusted OR 4.79, 95% CI 1.61–14.23, $P = 0.005$) for the late treatment group (Supplemental Table S3, S4, and S5). Concerning in-hospital mortality, our univariate analysis and multivariate regression model revealed that both groups did not significantly differ. After excluding 28 cases of postoperative in-hospital mortality, patients with acute myocardial ischemia in the late treatment group had a significantly higher incidence of postoperative stroke (29.4% ischemia, 8.9% no ischemia, $P = 0.002$) (Supplemental Table S6). Nevertheless, Kaplan–Meier analysis and log-rank test revealed no correlation between acute myocardial ischemia and long-term survival, regardless of the surgical timing (the early treatment group, HR 3.82, 95% CI 0.92–16.9,$P = 0.066$; the late treatment group, HR 4.16, 95% CI 0.96–18.0,$P = 0.056$). (Supplemental Figures S4 and S5).

DISCUSSION

Time to Surgery and the Surgical Time-Dependent Prognostic Relevance of ECG

Patients with acute myocardial ischemia have more preoperative complications than the non-ischemic group, which implies significant differences in 30-day mortality, in-hospital mortality, and long-term survival rates in those who received prompt surgical treatment within 7 h of symptom onset. Despite the different mechanisms, the analogous phenomenon by Goda et al. reported that neither cardiac tamponade nor shock is associated with in-hospital mortality [26]. The author attributed this to the shortened interval between hospital presentation and surgery initiation, reducing circulatory collapse time. Such ongoing hemodynamic instability might have pressured the medical staff to accelerate the pre-hospital patient transport, diagnostic workup at the emergency department, and consultation with cardiovascular surgery teams upon ATAAD confirmation. Therefore, the adverse prognostic impact of acute myocardial ischemia might be sharply diminished by rapidly establishing a cardiopulmonary bypass and promptly initiating the surgical repair. However, we must assert that this essentially observational study can only be interpreted within the scope of correlation or association and is not capable of constructing causal inference.

On the contrary, acute myocardial ischemia is independently associated with 30-day mortality and postoperative stroke in patients who did not undergo surgery within the 7-hour window. Furthermore, even though they survived until hospital discharge, approximately one-fourth of them had postoperative stroke complications during hospitalization. However, rather than a cause-and-effect relationship between acute myocardial ischemia and stroke, other reasons for postoperative stroke are plausible, such as dissection into the supra-aortic trunk and subsequent cerebral malperfusion.

Regarding long-term survival at 20 years after discharge, we observed no significant difference between patients with and without acute myocardial ischemia. In the subgroup analyses of both treatment groups, the results were also alike. Similar findings at the 5-year follow-up have been reported by Costin et al. [8].

The Heterogeneity of The Reported Incidence of ECG Abnormalities

Previous studies have reported acute myocardial ischemia incidence in patients with ATAAD ranging between 20–70% [4, 6, 8-19]. In this study, ATAAD was complicated by acute myocardial ischemia in approximately 30% of our patients on admission. Differences in adopted ECG morphology standards and variations in ECG acquisition timing across studies have resulted in a wide heterogeneity and a broad range of published figures [12, 16, 18, 19], making meaningful inter-study comparisons challenging.

Preoperative Characteristics

Regarding the systemic complications of ATAAD, previous studies have revealed that patients with acute myocardial ischemia have a higher incidence of cardiac tamponade and shock [8, 14-16, 18, 19]; however, this association was not observed in our study as the strongest independent factor for acute myocardial ischemia was a preoperative stroke. In patients with ATAAD presenting acute myocardial ischemia on admission, approximately one-fifth of them harbored acute coronary involvement. Underlying mechanisms of acute coronary involvement currently proposed in medical literature include (1) bulging of the highly pressurized false lumen that obscured proximal coronary trunks, (2) the free-floating of the sheared-off intimal flap at coronary orifices, and (3) retrograde extension of the dissection into the sinus of the Valsalva [11, 12, 14-16, 18, 19]. All these factors potentially lead to coronary orifice occlusion or intimal disruption of coronary arteries. This is followed by a compromised coronary blood supply, which can be detected in subsequent ECG displaying ischemic changes. However, in patients without acute myocardial ischemia and CT involvement of the aortic root, only 6.5% had acute coronary involvement intraoperatively in this study.

Study Limitations

This is the first study to emphasize the surgical time-dependent prognostic value of ischemic ECG abnormalities in patients with ATAAD; however, there were notable limitations. First, we conducted this retrospective study using medical records from a single tertiary referral hospital. Hence, patients who had died prior to arrival at our hospital were not included, probably leading to selection bias and underestimated mortality. Furthermore, the definition of "acute myocardial ischemia" used in this study is merely operational. It only denotes ECG ischemic signs and is a surrogate for actual ischemia. Third, calculating the time from symptom onset to operation was based on the subjective accounts of patients or their families. In patients with insidious symptom onset, precise estimation was challenging. Fourth, our results were derived from the retrospective analysis of ECG recorded on admission instead of ECG performed immediately before initiating the surgery.

CONCLUSIONS

Acute myocardial ischemia was unassociated with mortality in patients with surgical treatment within 7 h of symptom onset. Conversely, acute myocardial ischemia was an independent risk factor of the 30-day mortality and postoperative stroke in patients that underwent surgery outside the 7-hour window. Therefore, medical staff should be alert to acute myocardial ischemia detected on ECG in patients diagnosed with ATAAD, as this is a vital for acute coronary involvement that might co-exist in one-fifth of these patients. Concerning long-term outcomes, there was no significant difference in the 20-year survival between the ischemic and non-ischemic groups, regardless of the surgical timing.

DISCLOSURE STATEMENT

There are no conflicts of interest to declare.

DATA AVAILABILITY

The authors declare that all data supporting the findings of this study are available within the article and its supplementary information files.

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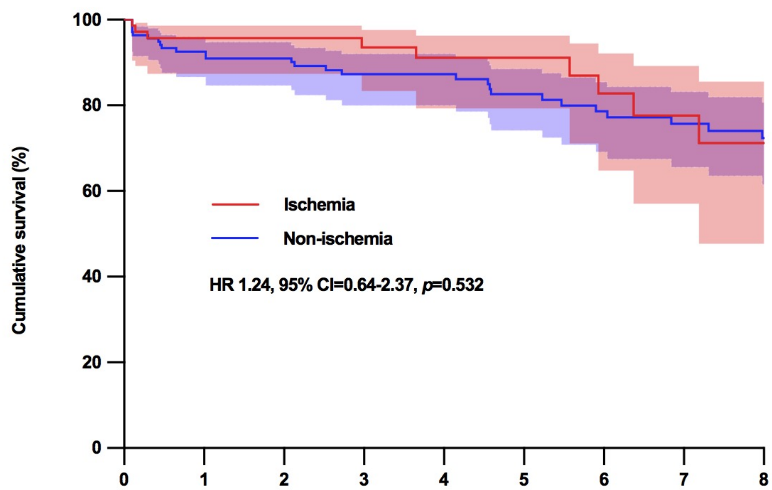
FIGURE LEGENDS

Graphical Abstract

Acute myocardial ischemia is associated with poor prognosis in patients receiving operation for acute type A aortic dissection beyond the initial 7 h.

Figure 1.

Legend: Time-to-Event Curves for Discharged Patients Previously Admitted due to ATAAD. Caption: Kaplan–Meier method and log-rank test were used to calculate the cumulative survival (y-axis) along the series of post-discharge years (x-axis) in patients with ATAAD, stratified by acute myocardial ischemia on admission. Notably, the median follow-up time was 4.15 years (0.00–21.13 years). Therefore, ATAAD indicates acute type A aortic dissection.



Number at Risk	0	1	2	3	4	5	6	7	8
Ischemia	72	63	49	44	31	27	20	15	10
Non-ischemia	139	118	103	89	79	65	58	50	44

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