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Original Research

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Off-hours Surgery and Mortality in Patients With Type A Aortic Dissection Repair: A Systematic Review and Meta-Analysis

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AUTHOR'S SUMMARY

In a systematic review and meta-analysis of 16,501 participants, a notable 'weekend effect' emerged for type A aortic dissection (TAAD) repair surgeries. Patients operated on during weekends faced a 41% higher in-hospital mortality risk compared to weekdays, while nighttime surgeries showed no increased risk. The study challenges previous categorizations of "overall off-hours" and highlights non-surgical concerns, like staffing or resources, during weekends. These findings underscore the need for hospitals to address weekend-specific challenges and advocate for more research to ensure consistent, high-quality care for TAAD patients round-the-clock.

ABSTRACT

Background and Objectives: The impact of off-hours admission (such as weekends, nighttime, and non-working hours) vs. regular hours (weekdays and daytime working hours) on the mortality risk of patients undergoing surgery for type A aortic dissection (TAAD) repair is still uncertain. To address this uncertainty, we undertook a comprehensive systematic review and meta-analysis. We aimed to assess the potential link between off-hours admission and the risk of mortality in patients undergoing TAAD repair surgery.
Methods: We conducted a thorough search of the PubMed, Embase, and Cochrane Library databases, covering the period from their inception to May 20, 2023. Our inclusion criteria encompassed all studies that examined the potential relationship between off-hour admission and mortality in individuals who had undergone surgery for TAAD repair. The odds ratios (ORs) were extracted and combined utilizing a random effects model for our synthesis.

of the study, the decision to submit for publication or approval of the manuscript for publication.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Chat GPT v.3.5 (Open AI, 2023) in order to check grammar. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the publication's content.

Conflict of Interest

The authors have no financial conflicts of interest.

Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization: Liu PPS, Loh CH; Data curation: Liu PPS, Hsu JY, Huang HK; Formal analysis: Liu PPS; Investigation: Liu PPS; Methodology: Liu PPS; Project administration: Liu PPS; Software: Liu PPS; Supervision: Yeh JI; Validation: Liu PPS, Chang JC; Visualization: Liu PPS; Writing - original draft: Liu PPS; Writing - review & editing: Liu PPS, Chang JC, Hsu JY, Huang HK, Loh CH, Yeh JI.

Results: Nine studies with 16,501 patients undergoing TAAD repair surgery were included in the meta-analysis. Overall, patients who underwent surgery during the weekend had higher in-hospital mortality (pooled OR, 1.41; 95% confidence interval [CI], 1.14–1.75; p=0.002) than those treated on weekdays. However, the mortality risks among patients who underwent TAAD surgery during nighttime and non-working hours were not significantly elevated compared to daytime and working hours admission.
Conclusions: Weekend surgery for TAAD was associated with a higher in-hospital mortality risk than weekday surgery. However, further studies are warranted to identify and develop strategies to improve the quality of round-the-clock care for patients with TAAD.

Keywords: Aortic dissection; Mortality; Postoperative complications

INTRODUCTION

Type A aortic dissection (TAAD) is a medical emergency requiring immediate surgical intervention.[1)2)] TAAD is characterized by its swift progression, often leading to fatal outcomes if not treated promptly. The high mortality rate associated with this condition underscores the paramount importance of timely and efficient surgical management. Previous studies have examined the higher mortality risk among patients who underwent TAAD repair surgery during off-hours, such as during weekends,[3)4)] nighttime,[5)6)] and non-working hours.[7)] However, worldwide evidence found the association between mortality risk and surgery time inconclusive.[8-10)] Consequently, this gap remains unclear and needs to be addressed.

A recent systematic review and meta-analysis study reported that out-of-hour admission was not associated with the 30-day mortality rate of patients with TAAD. However, the study categorized weekends and nighttime as "out-of-hour," which was not informative for improving hospital management.[11)]

Recently, several new studies have investigated the effect of off-hours on the mortality outcomes of patients with TAAD,[3-5)7-10)12-14)] and the number of studies and sample size has expanded beyond what was included in previous systematic reviews and meta-analyses.[11)] However, the association between off-hours surgery (including during weekend, nighttime, and non-working hours) and mortality among patients with TAAD remain inconclusive. A comprehensively updated systematic review and meta-analysis is still lacking.

Therefore, we performed a systematic review and meta-analysis to compare the mortality risk between patients who underwent TAAD repair surgery during off-hours and those treated during corresponding regular hours.

METHODS

Ethical statement

We registered the research protocol on the International Prospective Register of Systematic Reviews platform (registration number: CRD42022347227). Institutional ethical approval was not essential, as it was a meta-analysis of the data of published studies.

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Data sources and literature search

The current systematic review and meta-analysis was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and we stated the required items in an online appendix.[15] We searched targeted studies on the Cochrane Library, Embase, and PubMed from their inception until May 20, 2023.

We searched for articles using the following concept terms: "aortic dissection," "type A dissection," "off-hour," "weekend," "night," "holiday," and "mortality." Details of the keywords for search engines are presented in **Supplementary Table 1**. Additionally, we examined the bibliography listed in the relevant reports to include additional articles.

Study selection and inclusion criteria

Studies were included in the systematic review if the following criteria were met: 1) participants admitted with TAAD diagnosis and underwent TAAD repair surgery, and 2) outcome measurements included in-hospital mortality or 30-day mortality with sufficient data to calculate the risk estimates for comparing off-hours and regular hours. The definitions of off-hours and regular hours varied among the previous studies, and we categorized the comparisons into three major types: 1) weekend vs. weekday, 2) nighttime vs. daytime, and 3) non-working hours (weekday nighttime and the whole day on the weekend) vs. working hours (weekday daytime), as described in detail in **Supplementary Data 1**. We excluded review articles, meta-analyses, case reports, conference abstracts, editorials, letters, and correspondence.

Two reviewers (P.-P. L. and H.-K. H.) independently screened all articles to evaluate those that have relevant titles and abstracts. If a study was considered eligible by either reviewer, it was included for further full-text review. Two reviewers (P.-P. L. and H.-K. H.), then independently assessed the full texts of the studies, and any disagreement was resolved by discussion until consensus was reached among the members of the study team.

Study outcomes

The primary outcome measured was the in-hospital mortality risk, and the secondary outcome was the 30-day mortality risk. Comparisons were made between individual off-hours and corresponding regular hours, using weekend vs. weekday, nighttime vs. daytime, and non-working hours vs. working hours comparisons.

The definitions of types of off-hours and corresponding regular hours are shown in **Supplementary Data 1**. Briefly, 'Weekend' refers to Saturday and Sunday from 00:00 to 23:59, while 'weekday' refers to Monday to Friday from 00:00 to 23:59. Working hours refer to the time from 08:00 to 16:59, Monday to Friday, while non-working hours refer to the time from 17:00 to 07:59 on the next day, Monday to Friday plus whole day (00:00 to 23:59) of Saturday and Sunday. 'Nighttime' and 'daytime' refer to the time Monday to Sunday.

Data extraction and quality assessment

Two authors (P.-P. L. and H.-K. H.) independently extracted data using a prespecified standardized form, including author names, publication year, article type, country, geographic location, study design, source of data, observation period, patient source, the definition of TAAD, categories of off-hours and regular hours, sample size, mean age, the proportion of sexes, mortality type, mortality risk estimates, and confounders adjusted in statistical analyses. A third author (J.-Y. H.) independently assessed the accuracy of extracted data.

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Odds ratios (ORs) with 95% confidence intervals (CIs) were extracted to calculate effect size and standard error. When a study reported estimates from covariate-adjusted and propensity score matching/weighting models, we considered the latter to be less biased and preferred it for data synthesis in the meta-analysis. The most adequately adjusted estimates from these studies were used. If there were any missing data, we attempted to contact the authors for relevant information.

Study quality was assessed independently by two reviewers (P.-P. L. and H.-K. H.), using the Newcastle–Ottawa Scale (NOS) for observational studies.[16] When disparities appeared between the two reviewers, a third reviewer (J.-Y. H.) attended in the data extraction and quality assessment process to resolve the disparities.

Data synthesis and statistical analysis

ORs were synthesized to calculate the pooled ORs in our meta-analysis. Because the observational study results are usually affected by confounding factors, such as age, sex, time from symptom onset to receive surgery, malperfusion syndrome, operation time, and surgical procedure, we only synthesized the data with adjusted for at least age and sex. We evaluated the between-study heterogeneity using the I^2 statistic. Heterogeneity was considered low, moderate, and high for I^2 of <50%, 50–75%, and >75%, respectively.[17] We calculated the pooled OR and corresponding 95% CIs using the DerSimonian and Laird random effects model.

We conducted several subgroup analyses to determine whether different study-level factors influenced the pooled estimates. These subgroup analyses were conducted according to the mean or median age (<65 years or ≥65 years), the proportion of males (<50% or ≥50%), geographic region (Asia, North America, Europe, and multiple continents), length of the observation period (<10 years or ≥10 years), median year of the observation period (before 2009 or after 2010), number of total cases (<1,000 or ≥1,000, which was in-line with the setting of a previous meta-analysis study),[11] number of cases per observation year (<100 or ≥100, which representing the hospital's capacity in performing TAAD repair surgery), and the classifying reference for off-hours (date of arriving emergency department, time of starting surgery, or date of admission).

We conducted further subgroup analyses to determine whether the type of adjusted covariates influenced the pooled estimates. We classified the type of adjusted covariates as three major types 1) age and sex 2) pre-operation assessment, e.g. time from symptom onset to receive surgery and malperfusion syndrome 3) intra-operation procedure, e.g., operation time, repair area involved, cross-clamp time.

Potential publication bias was assessed using the Egger's test. We used a funnel plot to assess publication bias or small-study bias.[18]

All statistical tests were two-sided, and the results were considered statistically significant at $p<0.05$. All statistical analyses were conducted using R version 4.2.3 (R Core Team, Vienna, Austria).

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RESULTS

Search results

In total 77 relevant records were identified during the initial search. After excluding duplicated records and irrelevant article titles and abstracts, 21 potentially relevant studies were retrieved for a full-text review. In summary, 14 studies met the eligibility criteria for full-text review.[3-10)12-14)19-21)] The PRISMA flow diagram of article selection for meta-analysis is shown in **Figure 1**. Detailed information, such as age, sex, total number of enrolled patients, and characteristics of the studies, are summarized in **Supplementary Table 2**. The adjusted covariates for each cohort study are presented in **Supplementary Table 3**. The quality assessment results obtained using the NOS are summarized in **Supplementary Table 4**.

Notably, 9 out of 14 eligible studies reported the ORs after adjustment for confounders, and we only used these results to calculate synthesized ORs. The total number of patients with TAAD surgery enrolled in the present meta-analysis was 16,501.[3-10)21)]

Risk of in-hospital mortality associated with off-hours versus regular hours

Patients who underwent TAAD repair surgery during the weekend had a higher in-hospital mortality risk than those treated during weekdays (pooled OR, 1.41; 95% CI, 1.14–1.75; p=0.002) with low heterogeneity (I^2=31%). On the contrary, there was no observed higher risk associated with nighttime and non-working hours; the pooled ORs were 1.17 (95% CI, 0.60–2.27; p=0.638; I^2=56%) for nighttime vs. daytime, and 1.05 (95% CI, 0.60–1.83; p=0.866; I^2=0%) for non-working hours vs. working hours (**Figure 2**). No evidence of publication bias was detected according to the funnel plot and Egger's test (**Supplementary Figure 1**).

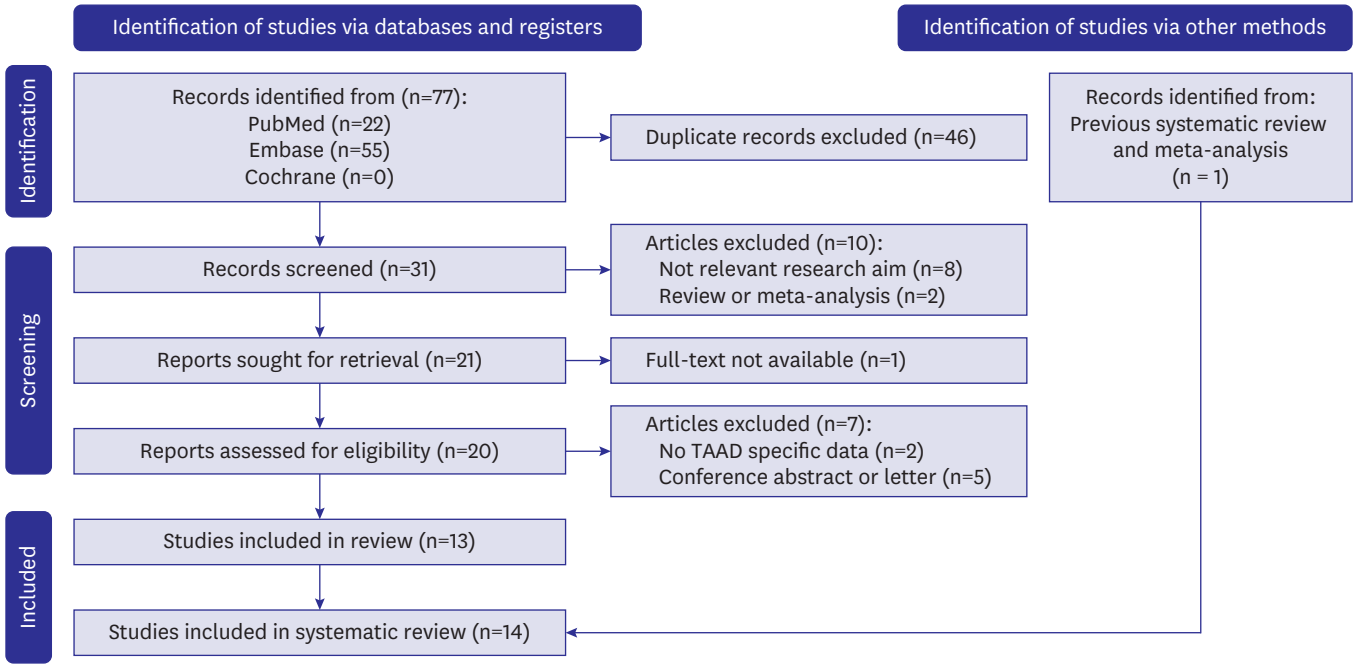

Figure 1. PRISMA flow diagram.
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; TAAD = type A aortic dissection.

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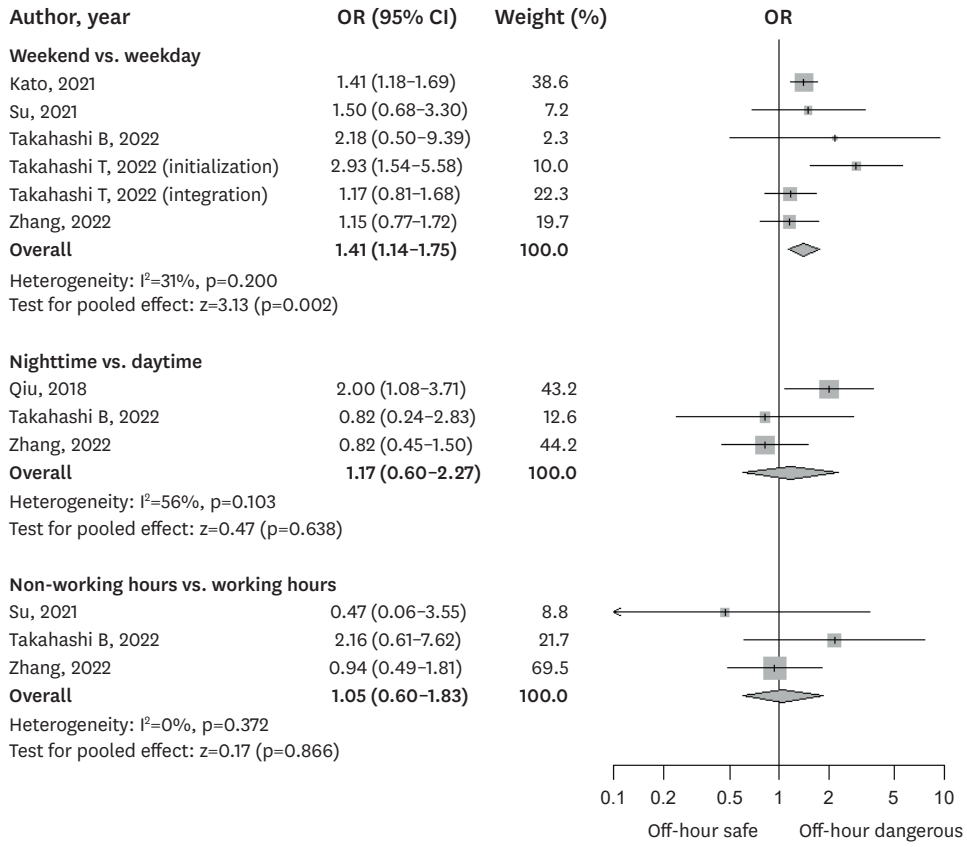

Figure 2. Forest plot of the OR of in-hospital mortality associated with individual off-hour effects.
CI = confidence interval; OR = odds ratio.

Subgroup analysis for in-hospital mortality associated with off-hours versus regular hours

The results of the subgroup analysis according to the study characteristics are shown in **Figure 3**, **Supplementary Figures 2** and **3**. The weekend effect was associated with a higher in-hospital mortality risk in the subgroups of elders (age ≥65 years), proportion of participants with males <50%, Asia countries, length of the observation period <10 years, median year of the observation period after 2010, number of total cases ≥1,000, number of cases per year ≥100 (**Figure 3**). The subgroup analysis results for the nighttime and non-working hour effects are shown in **Supplementary Figures 2** and **3**. The pooled risk of mortality was associated with neither nighttime nor non-working hours treatment (**Supplementary Figures 2** and **3**).

We performed subgroup analyses according to each study's adjusted severity-related covariates (age, sex, pre-operation assessment, and intra-operation procedure) (**Figure 4**). Patients undergoing weekend surgeries consistently showed a trend of higher mortality risk compared to those with weekday surgeries across different subgroups. Specifically, in the subgroup adjusted for age, sex, and pre-operation assessment, the pooled OR for weekend vs. Weekday surgeries was 1.51 (95% CI, 0.98–2.32; p=0.064; I^2=58%); when further adjusted for intra-operation procedures, the OR was 1.47 (95% CI, 0.91–2.39; p=0.114; I^2=70%).

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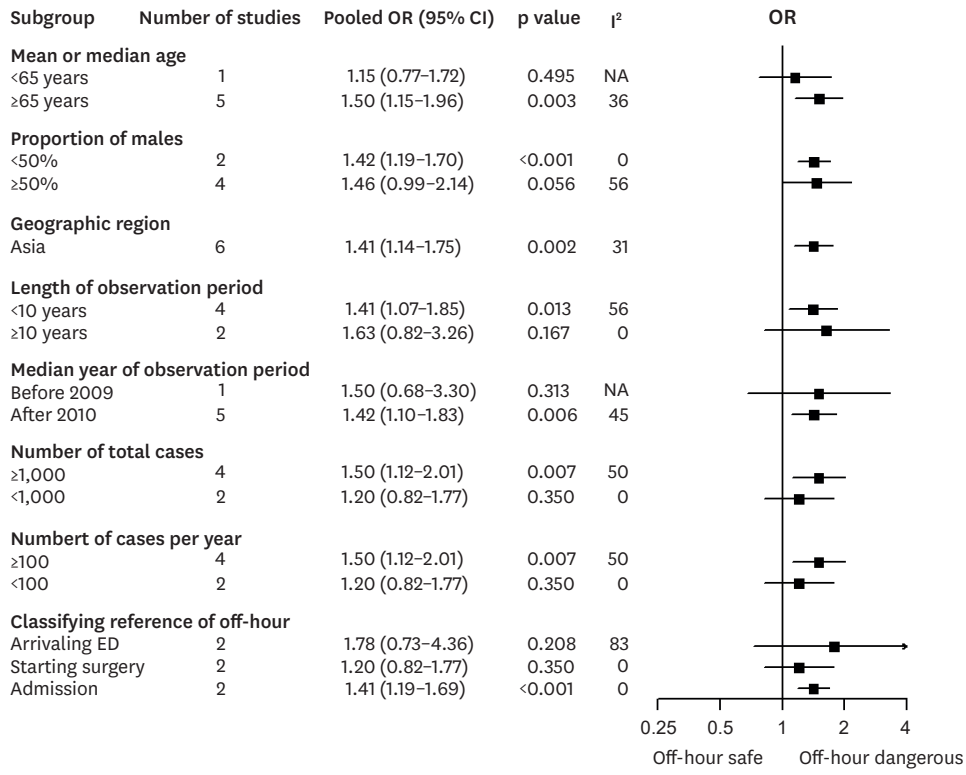

Figure 3. Subgroup analysis of pooled ORs of in-hospital mortality between weekend- and weekday-treated patients.
CI = confidence interval; NA = not available; OR = odds ratio.

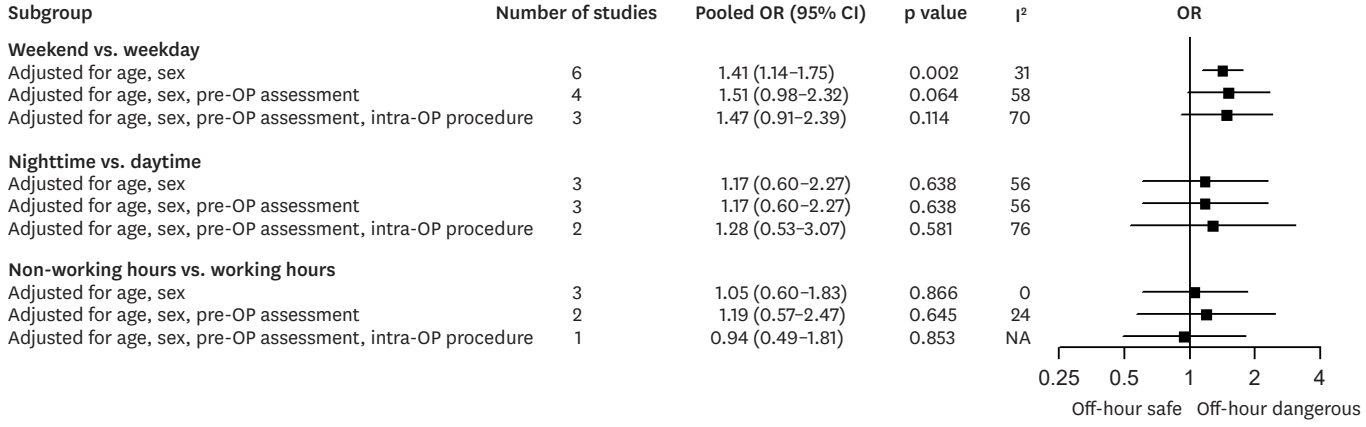

Figure 4. Sensitivity analysis of in-hospital mortality according to confounder component settings. pre-OP assessment only included the studies report adjusted results for pre-operation assessment, such as malperfusion syndrome, tamponade, cardiopulmonary arrest, or time from symptom onset to hospital arrival/surgery. Intra-OP procedure only included the studies report adjusted results for intra-operation procedure details, such as cardiopulmonary bypass time, aortic cross-clamp time, hypothermia circulatory arrest time, blood transfusion or replacement of total or hemi arch.
CI = confidence interval; OR = odds ratio; OP = operation.

Risk of 30-day mortality associated with off-hours versus regular hours

The pooled results and funnel plots for the analyses of 30-day mortality are shown in **Supplementary Figures 4** and **5**. The results suggest that there were no significant differences in the 30-day mortality between patients treated during weekends vs. weekdays (pooled OR, 1.97; 95% CI, 0.27–14.54; p=0.505), nighttime vs. daytime (pooled OR, 1.00; 95% CI, 0.26–3.78; p=0.996), and non-working hours vs. working hours (pooled OR, 1.01; 95% CI,

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0.18–5.50; p=0.993) (**Supplementary Figure 4**). No evidence of publication bias was detected according to the funnel plot and Egger's test (**Supplementary Figure 5**).

DISCUSSION

In the present meta-analysis involving 16,501 participants from 9 studies, we found that patients with TAAD repair surgery during the weekend had an overall 41% higher risk of in-hospital mortality than those who underwent surgery during the weekday. TAAD repair surgery during nighttime or non-working hours was not associated with in-hospital or 30-day mortality rate.

In our subgroup analysis, we found that after adjusting for different severity-related covariates (pre-operation assessment and intra-operation procedure), the pooled OR exhibited a consistent trend, showing a higher mortality risk for patients undergoing TAAD repair surgery during the weekend than for those admitted on weekdays. Therefore, this result indicated that the "weekend effect" on mortality risk might not completely be attributed to the disease severity or intraoperative procedure but could be related to factors, including hospital staffing, surgical room scheduling, and blood reserves. Further rigorous studies are needed to explore these factors that have yet to be comprehensively studied.

A previous systematic review and meta-analysis found that lower 30-day mortality was associated with in-hours surgical operation (pooled risk ratio, 0.81; 95% CI, 0.72–0.90; p<0.001),[11] and this study implied that a 10% higher mortality risk was associated with off-hours surgery. However, the classification method, which considered weekends to have the same effect as nighttime on the mortality of patients with TAAD surgery, was not practical; specifically, the differences in the off-hours per day, operation schedule, and duty arrangements between weekends and nighttime may be dissimilar. Another limitation is the absence of reporting on the association between various out-of-hour periods and in-hospital mortality rates. In life-threatening conditions such as TAAD, in-hospital mortality rates can more directly reflect the quality of medical care received by patients and the relationship between in-hospital factors (e.g., transfer, workforce, surgical team, and post-operation care capability) and in-hospital mortality rates. Therefore, we conducted separate meta-analyses to examine the effects of weekend and nighttime surgeries on the mortality rate of patients undergoing TAAD repair surgery. We observed a 41% higher mortality risk comparing weekend surgery to weekday surgery. This result indicated that we could put more effort into enhancing the necessary medical environment during the weekend.

Several possible mechanisms could explain the presence of the "weekend effect." TAAD is a critical condition that requires immediate surgical intervention. In practice, a rapid diagnosis and operation team are crucial factors in the survival of patients. Maintaining uniform quantity and quality of the medical staff throughout the week is difficult, and, typically, fewer hospital staff work during the weekends than on weekdays.[22] Insufficient staffing could result in fatigued healthcare professionals, and a smaller workforce has been reported to affect surgical intervention outcomes. Some studies have shown that the staff working on weekends were less experienced than those working on weekdays.[23][24] These factors exist simultaneously on weekends, which could possibly explain the difference in mortality outcomes between weekends and weekdays. Similarly, efficient and adequate nursing staff are essential for the quality of postoperative care.[25][26] Previous findings showed that there were fewer nursing staff on weekends than on weekdays, and there was an association between reduced nurse staffing and increased risk of mortality.[27]

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Previously, some studies suggested that patients undergoing TAAD repair surgery during off-hours had a higher severity of illness. Among the studies we included, some reported a higher proportion of out-of-hospital cardiac arrest, consciousness change, and malperfusion syndrome in patients who underwent TAAD repair surgery during the weekend.[4)7)] However, in other studies, no difference was found in the prevalence of tamponade, acute neuro complications,[7)] interfacility transfer, time from symptom onset to hospital arrival,[4)] acute kidney injury, or multisystem organ failure[10)] between patients admitted for TAAD surgery during the weekend and those admitted during weekdays. Therefore, further rigorous studies, particularly those collecting clinical factors and disease severity, will be necessary in the future to validate our findings.

The surgeon factor is thought to be a critical determinant for mortality for all major surgeries. Only one study[7)] enrolled in this work provided findings to assess the role of the surgeon factor. The authors showed that no differences were found in the volume per year and primary operator experience of cardiovascular surgeons between the regular-hour and off-hour groups, but the later study group had a higher rate of mortality (**Supplementary Table 5**). Thus, the surgeon factor appears to be not a crucial factor for the mortality in their study.

Establishing a rapid response team of cardiac surgeons to perform TAAD operations is very popular among hospitals in different regions. As such, our data indicated that the OR of mortality in the non-working hour group was not significantly increased when compared with the working hour group.

In TAAD repair surgery, the choice of replacement site (hemi-arch vs total arch) usually correlates with the location and size of the intimal tear, and the severity often relates to mortality outcomes. The proportion of patients undergoing total arch or hemi-arch replacement varied among the studies included in the current meta-analysis. Our analysis (**Supplementary Table 6**) revealed that only one study[7)] detected a mild difference in the surgery composition between surgeries performed during weekends and weekdays. Other comparisons show no remarkable differences in this aspect between off-hour surgeries and regular-hour surgeries in other included studies. Thus, the difference in surgical composition is unlikely a contributing factor to the mortality differences observed in this work.

We comprehensively evaluated the association between the off-hour effect and mortality risk in patients undergoing TAAD repair surgery. We found that those patients who received treatment during weekends had a higher mortality risk than those who underwent surgery on weekdays. Therefore, the potential disadvantages, including the medical environment, less experienced surgeons, insufficient nursing staff, and inadequate duty arrangements, need to be addressed.

There was an established solution that could improve the weekend effects at the frontline. The Tokyo Acute Aortic Super-network (TAAS), a coordination system between hospitals and pre-hospital emergency medical services, could rapidly assess and precisely transfer patients with suspected or confirmed TAAD to a suitable hospital for treatment.[4)] After five years of implementation of the TAAS program, the in-hospital mortality of patients admitted for TAAD during the weekend had a 40% reduction compared to that before the implementation. It achieved a similar mortality rate compared to admission during the weekdays. The TAAS was an excellent example demonstrating that building an efficient triage system and optimizing the transfer model could reduce the mortality risk of patients admitted with TAAD during the weekend.[4)] We highlighted this successful model that can

reduce the mortality rate of patients with TAAD repair surgery during weekends. Multi-domain inputs are needed to improve the survival outcome of patients with TAAD.

This systematic review and meta-analysis have some limitations. First, only nine studies reported the adjusted mortality risk estimate for the off-hours effect and were included in the meta-analyses.[3-10)21)] Despite our efforts to access the latest and most comprehensive research findings, the number of enrolled studies included in the meta-analysis for the effects of weekends (n=6), nighttime (n=3), non-working hours (n=3) seemed insufficient. The lack of statistical power may affect our evaluation of off-hours' effect on the mortality of patients with TAAD. More studies are needed to evaluate the effect of off-hours on the mortality of patients with TAAD. Second, although the studies included in our meta-analysis accounted for the influence of confounding factors on the results, the specific covariates adjusted for in each study were not entirely consistent. Therefore, future research should focus on prospective and standardized studies for more accurate results, and we recommend the development of more databases to investigate the comprehensive contents. Thirdly, there were few studies that encompassed both preoperative assessment and intraoperative procedures. In the subgroup analysis of these studies (n=3), the OR was 1.47 (95% CI, 0.91–2.39; p=0.114) for in-hospital mortality outcome despite not achieving statistical significance. However, the meta-analyses conducted thus far may be susceptible to the limitations imposed by a small number of included studies, resulting in inadequate statistical power. Lastly, the medical standards may vary across countries and regions and may impact the outcomes following TAAD surgery. The studies included in this meta-analysis were mostly conducted in East Asian countries (Taiwan, Japan, and China). As such, our findings cannot be generalized to other countries or regions. Through our systematic review and meta-analysis, we present current evidence that demonstrates a potential correlation between weekend surgery and an elevated risk of in-hospital mortality for patients with TAAD.

In conclusion, this systematic review and meta-analysis obtained data from 16,501 participants from 9 studies and demonstrated that patients who underwent TAAD repair surgery during weekends had a 41% higher risk of in-hospital mortality than those who underwent operation on weekdays. Further studies are required to determine the mechanisms underlying these effects and to devise a solution to improve the quality of round-the-clock care for patients with TAAD.

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SUPPLEMENTARY MATERIALS

Supplementary Data 1

Types of off-hours and corresponding regular hours

Supplementary Table 1

Search strategies

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Supplementary Table 2
Summary of the studies included in the present systematic review

Supplementary Table 3
Covariates adjusted of the studies included in the systematic review

Supplementary Table 4
Quality assessment of the studies included in the present meta-analysis using the Newcastle–Ottawa Scale

Supplementary Table 5
Experience characteristics of primary surgeon performing type A aortic dissection repair surgery

Supplementary Table 6
Proportion of receiving total arch replacement among patients with TAAD in previous studies

Supplementary Figure 1
Funnel plot for publication bias in studies comparing in-hospital mortality associated with individual off-hour effects. The Egger's test p values were 0.483, 0.815, and 0.991 for weekend, nighttime, and non-working hours subgroups, respectively.

Supplementary Figure 2
Subgroup analysis of pooled ORs of in-hospital mortality comparing nighttime- and daytime-treated patients.

Supplementary Figure 3
Subgroup analysis of pooled ORs of in-hospital mortality comparing non-working hours- and working hours-treated patients.

Supplementary Figure 4
Forest plot of the OR of 30-day mortality associated with individual off-hour effects.

Supplementary Figure 5
Funnel plot for publication bias in studies comparing 30-day mortality associated with individual off-hour effects. The Egger's test p value was 0.521 for the nighttime subgroup.

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