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Nocturnal elective coronary artery bypass grafting (CABG) surgery is not associated with increased one-year mortality

Andreas Koköfer^{1*}, Christian Dinges², Crispiana Cozowicz¹, Bernhard Wernly^{3,4} and Niklas Rodemund¹

Abstract

Background Elective coronary artery bypass grafting (CABG) surgeries are increasingly scheduled during nighttime or after-hours. This poses unique challenges, such as reduced staffing, disrupted circadian rhythms, and increased fatigue, which may potentially affect outcomes. Despite growing evidence on the impact of daytime on cardiac surgery outcome, results remain inconclusive. The current study aims to investigate a potential association between surgery timing (daytime: 7:00 AM to 7:00 PM vs. nighttime: 7:00 PM to 7:00 AM) and long-term survival in patients undergoing elective CABG.

Methods In this retrospective single-institution cohort study at the University Clinic Salzburg, Austria, we analyzed elective CABG surgeries performed between January 1, 2017, and December 31, 2021. The primary hypothesis was that nighttime elective CABG surgeries have worse long-term survival. Among 2,179 cardiac surgical procedures, 723 elective CABG surgeries were identified and analyzed. Long-term survival was assessed using Cox proportional hazard modeling, while secondary outcomes, including 30-day and one-year mortality rates, were evaluated through multiple linear regression analysis.

Results The one-year mortality rate was 2.6% ($n = 19$) for the observation period. Of the 723 patients, 646 (89.35%) underwent daytime surgery, and 77 (10.65%) had nighttime surgery. The median EuroScore II was 1.50 [1.00, 2.60] for daytime surgeries and 1.70 [1.10, 3.10] for nighttime surgeries ($p = 0.111$). There was no association between nighttime surgery and long-term mortality (aHR: 1.624, 95% CI: 0.589 to 3.662, $p = 0.3179$). Multivariable logistic regression analysis confirmed that nighttime surgeries were not significantly associated with increased one-year mortality (aOR: 1.089, 95% CI: 0.208 to 3.711, $p = 0.905$). No deaths occurred within 30 days in either group.

Conclusion This analysis found no significant association between nocturnal elective CABG operations and increased long-term or one-year mortality. This study did not aim to evaluate the economics of nocturnal surgeries at the investigated institution. To confirm our results that there is no increased morbidity and mortality associated with nocturnal CABG operations, and to understand the economic impact of nocturnal surgeries, prospective randomized studies would be necessary.

Keywords Cardiac surgery, CABG, Night time, Long term survival, Cox proportional hazard model

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Introduction

Annually, 18 million Americans are diagnosed with coronary artery disease (CAD), the most common cause of death in the United States [1]. Globally, the number of CAD is increasing [2]. Despite advancements in the medical and interventional management of CAD, Coronary Artery Bypass Grafting (CABG) remains a crucial pillar in the treatment of obstructive coronary artery disease, particularly for patients with multivessel disease or diabetes [3]. Therefore, isolated CABG is by far the most common cardiac surgical procedure in the United States with 157,704 cases in 2018 [4]. This number underscores CABG's vital role in the management of complex coronary artery diseases.

CABG surgeries stand as a cornerstone in the management of complex coronary artery disease and are performed with varying degrees of urgency, including both emergent and planned interventions [5]. In the interest of optimizing surgical scheduling and mitigating the high demand for daytime operating facilities, there is a growing trend towards conducting elective CABG procedures during off-peak hours [6]. This shift to after-hours surgeries introduces distinctive considerations, including limited staff availability, perturbation of natural sleep-wake cycles, changed team dynamics, and the potential for increased clinician fatigue—all of which may influence the quality and safety of patient care [7, 8]. As such, this approach necessitates a careful evaluation of its implications on perioperative outcomes [9–11]. The scheduling of cardiac operations, particularly with regard to their timing, has been the subject of extensive research [3, 6]. Despite this, the outcomes of such studies have yet to yield a consensus, leaving the impact of surgery timing on patient outcomes an open question within the medical community. This ambiguity underscores the need for continued investigation into the optimal timing of cardiac surgeries to ensure the highest standards of patient care and safety [6, 7, 12]. A prevalent limitation of numerous investigations into cardiac surgery outcomes is their narrowed focus on short-term metrics, predominantly 30-day mortality rates [13]. Such a scope may not capture the full spectrum of factors critical to long-term patient survival, particularly in the context of CABG where the integrity of anastomoses plays a pivotal role in patient prognosis well beyond the initial postoperative period. Acknowledging this gap, the present study aims to explore the influence of operative timing by comparing daytime surgeries (7:00 AM to 7:00 PM) and nighttime surgeries (7:00 PM to 7:00 AM) on the long-term survival of patients who undergo elective CABG, thereby providing a more comprehensive understanding of the temporal dimension in surgical outcomes.

Methods

Study population and data sources

This retrospective cohort analysis included patients who underwent elective CABG surgery utilizing cardio pulmonary bypass (CPB) at the General Hospital Salzburg, Paracelsus Medical University from 2017 to 2021. The primary outcome of this study was the long-term mortality (as described below), depending on whether the surgical procedure was performed during daytime or nighttime. Any surgery was classified as a nighttime operation if either the start or end of the operation, or both, fell within the respective time period. Secondary outcomes encompassed one-year mortality and 30-day mortality. In addition, the severity of patients' conditions in the Intensive Care Unit (ICU) was evaluated using the SAPS 3 score [14, 15] at the time of ICU admission. We also analyzed the incidence of acute kidney injury (AKI), classified according to the KDIGO definition [16] during the ICU stay, and measured the high sensitivity Troponin T (hsTnT) plasma concentrations on the day of admission and on the first postoperative day. Perioperative data was extracted from the institutional Salzburg Intensive Care database (SICdb) [17]. SICdb was implemented using data from the hospital ICU data management system (PDMS) iMDsoft MetaVision ICU (iMDsoft, Needham, MA) and the electronic health record (EHR) ORBIS (DH Healthcare GmbH, Bonn, Germany). The database contains admission, discharge, surgical procedural and ICD10 data. Additionally, medications (including dosage), procedures such as renal replacement therapy (RRT), intubation etc. are reported in SICdb. SICdb (Version 1.0.6) was queried in 05/2023, completing entries up to and including 12/2021 were evaluated. Data on long-term mortality are currently not reported in SICdb. Therefore, those were collected from Austria's Federal Statistical Office (Statistik Austria, German: Bundesanstalt Statistik Österreich). Data was accessed on 01/2023. All data are fully anonymized as defined by the European General Data Protection Regulation [18]. The deidentification strategy of all data sources additionally complies with the 'Guidance Regarding Methods for Deidentification of Protected Health Information in Accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule' [19]. Reporting standards set by the REporting of studies Conducted using Observational Routinely-collected health data (RECORD) initiative were followed (see Appendix 1) [20]. The study was approved by the State Ethic Commission of Salzburg, Austria. (EK Nr: 1115/2021). Given the sole use of de-identified data, no written informed consent was required.

Statistical analysis

All patients within SICdb who had any cardiac surgery using CPB were included in the analysis. Subsequently, patients who had procedures other than isolated CABG, were excluded. Similarly, all emergency surgical procedures were excluded from the analysis. Figure 1 illustrates the STROBE diagram, detailing the patient selection process and exclusion criteria. During the study period, no patients under the age of 18 were operated on.

Continuous data points were expressed as median $\pm$ interquartile [IQR] range. Categorical data were stated in numbers (percentage). Univariable distribution differences between groups were calculated using the Chi-square test, Student t-test, Mann-Whitney U test, and Kruskal-Wallis test, depending on distribution, respectively.

Missing values for continuous variables were imputed by a best subset multiple regression. The results of the analyses were confirmed by the method of multiple imputation. Multivariable survival analysis was performed

using Cox proportional hazard regression. Due to the relatively small number of patients in the elective CABG group and the corresponding rare event of death, Firth's correction procedure [21] as suggested by Puhr et al. [22] was applied to the regression modelling. Although the populations in the univariate analysis were very similar, potential selection bias was addressed by including the EuroScore II [23] as independent variable in the Cox proportional hazard model. Adjusted Hazard Ratios (aHR) with respective 95% confidence intervals (95%CI) have been reported for the Cox proportional hazard model together with model fit statistics and *p*-values. Multivariable linear regression analysis was used to analyze the secondary outcome 'Death within one year after surgery'. Again, Firth's procedure as penalized maximum likelihood was applied to correct for small numbers. Similar as in the Cox proportional Hazard analysis the EuroScore II [23] was used as independent variable to correct for any selection bias or preexisting comorbidities. We reported adjusted odds ratios (aOR) with respective 95%

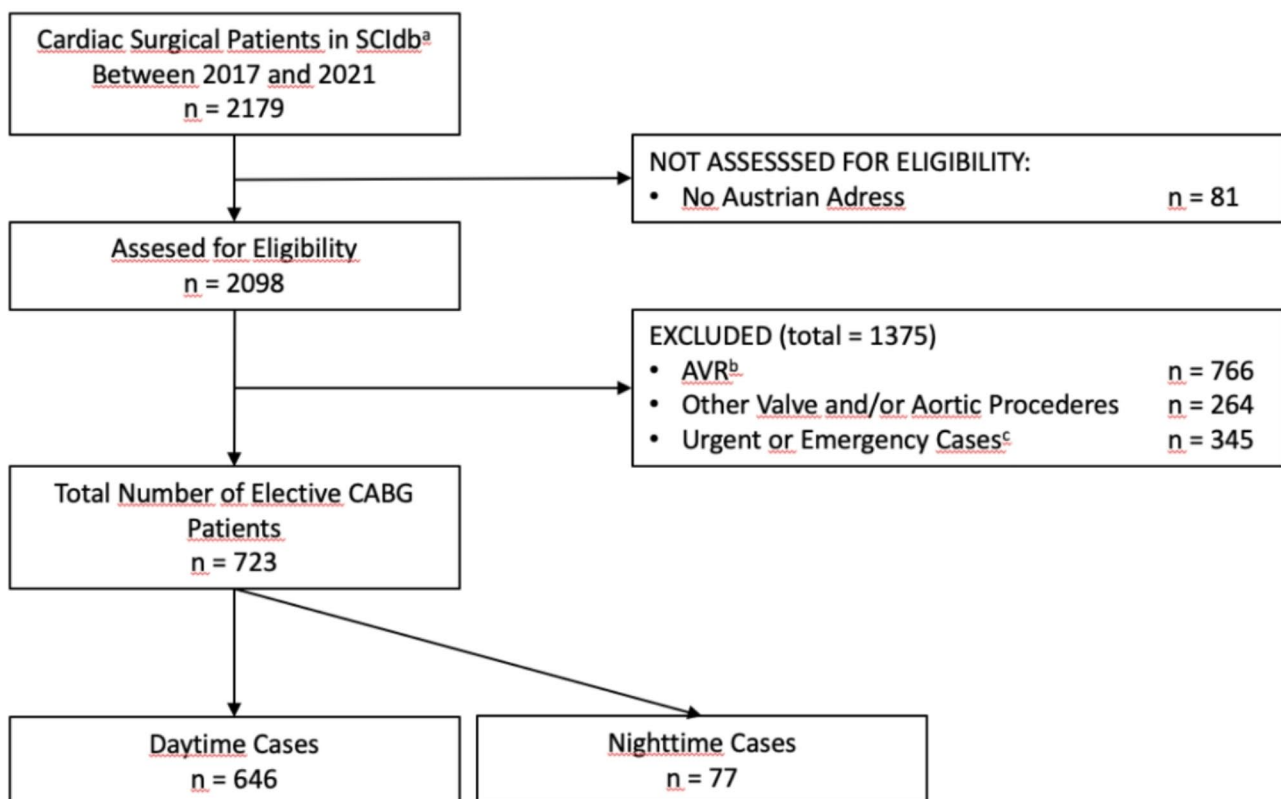


Fig. 1 Presents the STROBE diagram for the selection of Coronary Artery Bypass Grafting (CABG) patients from the Salzburg Intensive Care Database (SICdb) over a five-year span from 2017 to 2021. The initial cohort comprised 2,179 individuals, from which 81 were immediately deemed ineligible due to the lack of an Austrian address. Following the eligibility assessment and the application of exclusion criteria, the total eligible patient count stood at 723. Exclusion criteria included patients undergoing Aortic Valve Repair (AVR), which encompasses all forms of aortic valve repairs such as those performed via Sternotomy, Hemisternotomy, Right Anterior Thoracotomy, etc. Additionally, urgent or emergency cases, which refer to all non-elective forms of surgery, were excluded from the study

^a SICdb: refers to the Salzburg Intensive Care Database

^b AVR: denotes Aortic Valve Repair and includes all forms of aortic valve repairs (e.g., via Sternotomy, Hemisternotomy, Right Anterior Thoracotomy, etc.)

^c Urgent or Emergency cases include all non-elective forms of surgery

confidence intervals (95%CI) for the multivariable model. All statistical tests were two-sided, a p -value of <0.05 was considered statistically significant. The R Project for Statistical Computing (RCore Team, 2022) was used for all statistical analyses. Survival analysis was conducted using the 'survival package', and Firth's Bias-Reduced Logistic Regression was conducted using the 'logistf package', respectively. (<https://cran.r-project.org>). Results were visualized using R Studio (RStudio Team Version 2022.12.0 + 353, 2022, Boston, MA).

Results

For this study, 2,179 cases were initially considered. After applying exclusion criteria and handling missing data, the final cohort for analysis included 723 cases. Among these, 646 patients underwent daytime surgery and only 77 had nighttime surgery (Fig. 1). Baseline characteristics of both groups were comparable across in virtually all relevant parameters (Table 1). The median EuroScore II was 1.50 [1.00, 2.60] in the daytime group and 1.70 [1.10, 3.10], $p=0.111$ in the nighttime group, respectively. Notably, there were no deaths within 30 days in both groups. The one-year mortality rate was 2.6% ($n=19$) overall, with a mortality rate of 6.6% ($n=48$) during the full observation period (median 1170 days [668, 1569]; censored 675 days (93.36%). The association between night-time surgery and increased hazard of death was not statistically significant (aHR: 1.624, 95% CI: 0.589 to 3.662, $p=0.3179$). There was a 13.1% increase in hazard in the survival analysis for each unit increase in EuroScore II ($p<0.001$) in the entire cohort. Survival curves and corresponding statistics for both day and nighttime surgeries are displayed in Fig. 2. The model's likelihood ratio test yielded a chi-square statistic of 27.60 on 2 degrees of freedom, with a p -value of <0.001 , suggesting

the model is a good fit for the data. The Wald test showed a chi-square statistic of 43.70 on 2 degrees of freedom, again with a p -value <0.001 , further supporting the model's significance. Table 2 details the overall mortality differences and at one-year after surgery, respectively. Multivariable logistic regression analysis revealed that the likelihood of one-year mortality was not significantly associated with night-time surgeries (aOR: 1.089, 95% CI: 0.208 to 3.711, $p=0.905$). An increase in EuroScore II was again associated with a significant increase in the odds of one-year mortality (aOR: 1.179, 95% CI: 1.102 to 1.262, $p<0.001$). Other secondary outcomes are presented in Table 2. Interesting observations include a shorter cross clamp time during nighttime surgeries, yet higher SAPS III scores and higher maximum serum concentrations of hsTnT in these patients at arrival at the ICU.

Discussion

In our study of 723 patients who underwent elective, planned CABG surgery, we found no significant difference in long-term survival rates between surgeries performed at daytime and those performed at night. Additionally, we observed no disparity in mortality within the first-year after surgery. To the best of our knowledge, this is the first study exploring long-term survival in patients who have undergone elective nocturnal CABG.

The study has several implications: Firstly, there is a lack of consensus in the literature regarding the temporal relationship between surgical timing and outcomes. A recent meta-analysis and post-hoc analysis by Fudulu et al. [7] suggested that suspected outcome differences based on circadian rhythms in cardiac surgery, depending on the time of day, are not significantly pronounced in aortic valve replacement (AVR) and CABG.

Table 1 Preoperative baseline characteristics of the study population

	Daytime Surgery ($n=646$)	Nighttime Surgery ($n=77$)	p
Height (median [IQR])	170.00 [165.00, 175.00]	170.00 [165.00, 175.00]	0.642
Weight (median [IQR])	80.00 [70.00, 90.00]	80.00 [70.00, 90.00]	0.440
Age (median [IQR])	70.00 [60.00, 75.00]	70.00 [60.00, 75.00]	0.724
Male (n (%))	535 (82.8)	62 (80.5)	0.731
EuroScore II ^a (median [IQR])	1.50 [1.00, 2.60]	1.70 [1.10, 3.10]	0.111
Preexisting Conditions			
Lung Disease (n (%))	63 (9.8)	4 (5.2)	0.273
Art. Hypertension (n (%))	96 (76.8)	54 (70.1)	0.249
Diabetes (n (%))	184 (28.5)	24 (31.2)	0.720
Renal Dysfunction (n (%))	81 (12.5)	16 (20.8)	0.067
Hemoglobin preoperative (g/dl) (median [IQR])	13.40 [12.60, 14.40]	13.50 [12.00, 14.40]	0.515
Premedication			
Betablockers (n (%))	415 (64.2)	42 (54.5)	0.123
ACE Inhibitors (n (%))	267 (41.3)	29 (37.7)	0.620
Statins (n (%))	493 (76.3)	56 (72.7)	0.579

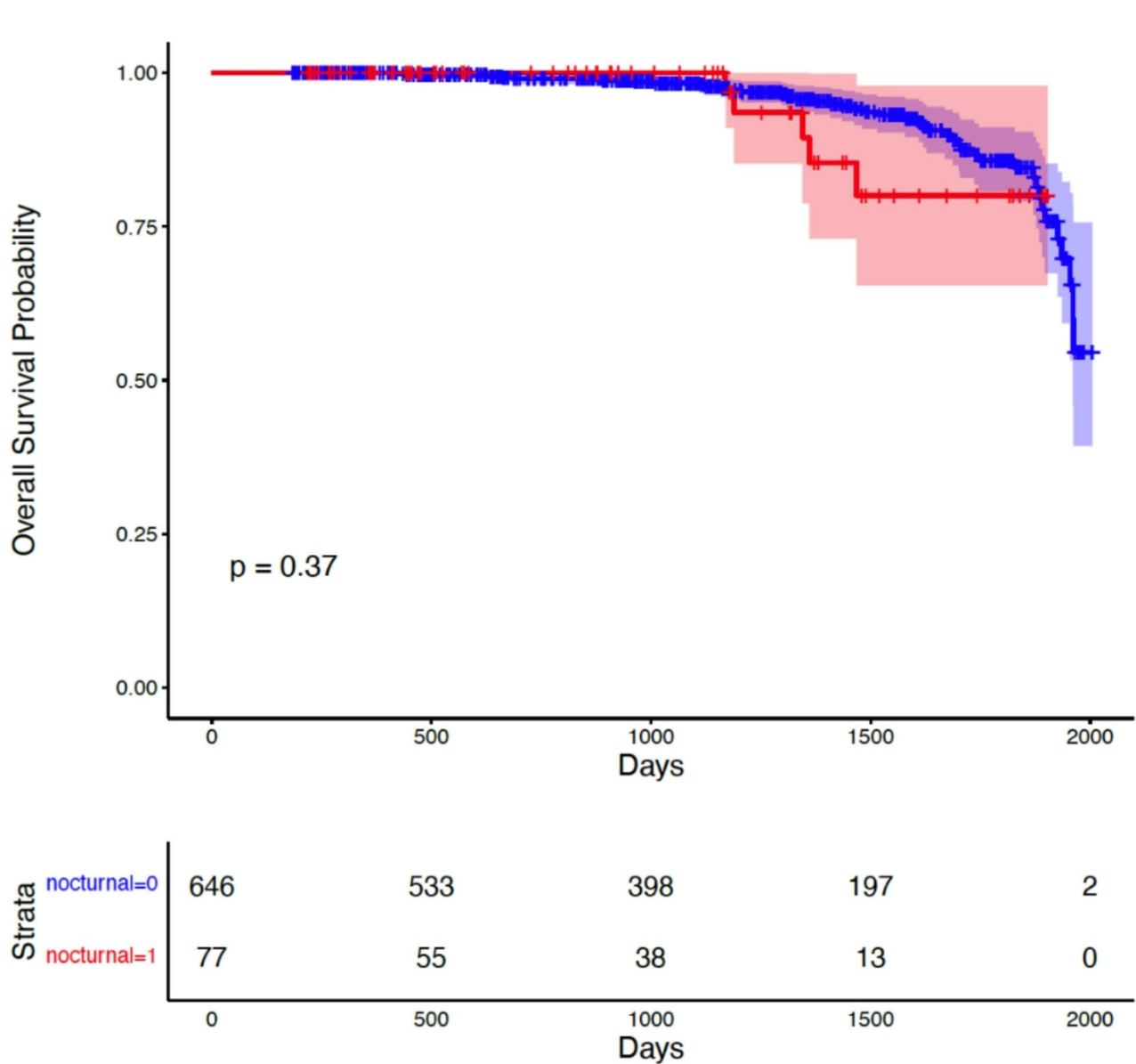


Fig. 2 Displays the Kaplan-Meier survival curves for CABG surgeries conducted at daytime (Nighttime_CABG=0) and at night (Nighttime_CABG=1). The plot depicts the decline in survival probability over time for both groups. The 95% confidence intervals are shaded in blue and red, respectively. The curves suggest similar survival probabilities for both groups across the observed time periods. The table details the number of patients remaining at risk at specified time intervals (0, 500, 1000, 1500, 2000 days) for surgeries performed during both daytime and nighttime

However, it is a plausible hypothesis that nighttime operations may carry an increased risk of errors attributable to fatigue among surgeons and their teams. Supporting this, Whitlock et al.'s retrospective analysis of the National Anesthesia Clinical Outcomes Registry data from 2015 indicates a notable correlation between post-6:00 pm surgery start times and elevated mortality risk, with the odds ratio calculated at 3.98 (95% CI: 1.54 to 10.3, $p=0.004$). This finding suggests that the timing of surgical procedures could be a significant independent factor affecting patient outcomes [24]. Similar findings were reported by Sinha et al. [25]. While specific data

on individual surgeons' performance during nocturnal hours are limited, it is reasonable to extrapolate that the observed trends in surgical outcomes might extend across different surgeons and healthcare professionals. The body of surgical literature presents a wide spectrum of results concerning the timing of procedures. Notably, Althoff et al. conducted a meta-analysis spanning various surgical specialties, suggesting an association between surgeries performed at night and a higher incidence of adverse outcomes. This supports the notion that the time of surgical intervention may be a crucial factor in determining patient prognosis [9]. This is corroborated by a

Table 2 Main outcome parameters: primary and secondary outcomes in the population; early postoperative indicators including SAPS3 score upon ICU admission and pertinent lab values (SAPS 3: simplified acute physiology score III; CPB: cardiopulmonary bypass; PRBC: packed red blood cells; AKI: acute kidney injury; KDIGO: kidney disease: improving global outcomes)

	Daytime Surgery (n = 646)	Nighttime Surgery (n = 77)	p
Deceased with 30 days after Surgery (n (%))	0 (0)	0 (0)	na
Deceased within one year after Surgery (n (%))	17 (2.6)	2 (2.6)	1.000
Deceased during the observation period (n (%))	43 (6.7)	5 (6.5)	1.000
SAPS 3 (median [IQR])	38.00 [33.00, 43.00]	41.00 [37.00, 47.00]	0.001
Cross Clamp Time (min.) (median [IQR])	52.50 [37.00, 68.75]	49.00 [33.00, 61.00]	0.049
CPB Time (min) (median [IQR])	97.50 [71.25, 125.00]	91.00 [67.00, 110.00]	0.059
Hs TnT d0 (ng/L) (median [IQR])	832.00 [516.25, 1320.00]	1025.00 [593.00, 1676.00]	0.077
Hs TnT d1 (ng/L) (median [IQR])	515.00 [308.50, 828.00]	725.50 [424.25, 1235.00]	< 0.001
Days of stay at the ICU (median [IQR])	3.04 [2.04, 4.17]	3.75 [2.75, 4.92]	0.453
Lactate avg. d0 (mmol/l) (median [IQR])	1.51 [1.31, 1.78]	1.52 [1.36, 1.78]	0.559
Lactate avg. d1 (mmol/l) (median [IQR])	1.24 [1.06, 1.45]	1.29 [1.10, 1.44]	0.701
Hematocrit min. d0 (%) (median [IQR])	26.00 [23.00, 30.00]	26.00 [22.00, 29.00]	0.365
Hematocrit min. d1 (%) (median [IQR])	28.00 [24.00, 31.00]	26.00 [23.00, 29.00]	0.002
Hemoglobin min. d0 (g/dl) (median [IQR])	8.90 [7.80, 10.10]	8.80 [7.60, 9.70]	0.285
Hemoglobin min. d1 (g/dl) (median [IQR])	9.20 [8.00, 10.20]	8.70 [7.88, 9.93]	0.108
PRBC d0 (median [IQR])	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.829
PRBC d1 (median [IQR])	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.825
Severe AKI (KDIGO ≥ 3) (n (%))	12 (1.9)	2 (2.6)	0.994

cardio-surgical retrospective analysis conducted with data from the University of Virginia, which indicated worse outcomes for night surgeries [26]. In contrast, a retrospective analysis by Axtell et al. conducted with data from 2,463 patients from the Corrigan Minehan Heart Center at the Massachusetts General Hospital, showed no differences in perioperative outcomes, operative mortality, length of stay, or total hospital cost for elective cases that start after 3 pm [27].

We did not focus on short-term outcomes in our study. Due to the overall low mortality rate following CABG, demonstrating such effects would have required a much larger number of patients and associated deaths, particularly in the nocturnal CABG group. Rather, we hypothesized that nocturnal operations might lead to poorer quality of anastomoses and consequently worse long-term survival due to the fatigue of the surgeon and the operating team. Fortunately, we were unable to confirm this assumption.

Our retrospective study, while insightful, is subject to several limitations intrinsic to its design. The lack of randomization, typical of observational studies, precludes drawing definitive causal inferences, warranting a prudent approach to interpreting observed associations. Selection bias is an endemic risk in any retrospective analysis. To address this, we incorporated the EuroScore II as a covariate for adjustment. Notably, our patient cohorts were comparably matched on all preoperative variables. This method stands in contrast to propensity score analysis, which often relies on a set of arbitrarily chosen variables and may introduce bias, particularly in survival studies. We posit that adjustment using a

repeatedly validated risk score may offer a more robust correction method in this context [28]. Additionally, our study did not investigate the economic implications of an elective planned nocturnal CABG operation. Our analysis reflects the experience of a single center, which may not be universally applicable. At our institution, it is uncommon for a surgeon to operate on more than one CPB case per day, meaning surgeons generally do not perform two consecutive CABG operations. Which in turn means that the surgeon who operated the nocturnal case was usually well-rested. The same applies to OR and anesthesia nursing, perfusionists, and intensive care nursing. Both the qualification and the number of involved personnel were identical between the day and night groups. However, there was no uniform model for anesthesiologic medical care. As data basis, we used the institute's own dataset (SICdb). The use of such preexisting registry of perioperative data and demographic information might lead to ambiguous definitions of disease; for example, chronic lung disease may encompass a known diagnosis of asthma or COPD or simply a history of pneumonia. Additionally, the varying complexities of cases between day and night could have affected the scheduling of surgeries. Therefore, an analysis that included the number and types of anastomoses, or the identity of the surgeon, might have provided further insights into the results. However, detailed information about the anastomoses was not available in the database. We did not use data on the individual surgeons due to the small number of operators and associated data privacy concerns. The distinction between night and day in our study was arbitrarily defined. In our case, we identified

the period between 7:00 PM and 7:00 AM as nighttime. This definition varies in other studies [5–10]. Due to the scheduling practices at our department, the number of patients operated on during nighttime hours was small. This, could be a potential source of bias too. The categorization into daytime and nighttime groups might have concealed insights from more precise time intervals, like the analysis of outcomes specifically during the period from midnight to the following morning. Lastly, we did not measure outcome measures other than death such as patient satisfaction, time to return to normal function, and longer-term morbidity, which can indicate the longevity of the bypass. Similarly, we were unable to collect data on the number of cardiological follow-up interventions (e.g., due to bypass occlusion). It must be emphasized that the mortality in our study may not only be caused by the CAD. Given the high average age of the patients, it is possible that deaths occurred due to other disease not directly related to CAD, such as oncological diseases or strokes. Future investigations into this topic would benefit from a prospective analysis: Alongside mortality, factors such as hospital costs, patient satisfaction, and longer-term follow-up, including subsequent cardiological interventions, should be assessed, as well as the quality of the surgical anastomoses and the CABG procedure itself.

Conclusion

Nocturnal elective CABG operations were not associated with increased long-term mortality in this analysis. Similarly, no association was found between nocturnal CABG operations and one-year mortality. This study did not aim to evaluate the economics of nocturnal surgeries at the investigated institution. To confirm our results that there is no increased morbidity and mortality associated with nocturnal CABG operations, and to understand the economic impact of nocturnal surgeries, prospective randomized studies would be necessary.

Author contributions

AK conceptualized the manuscript, did the statistical analyses and wrote the manuscript; NR generated the SICdb dataset and reviewed the manuscript; CD reviewed the manuscript; BW supported the descriptive analysis and reviewed the manuscript; CC helped to prepare the manuscript and reviewed the manuscript; All authors agree to be accountable for all aspects of the work in ensuring accuracy and integrity of the work.

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Data availability

The SICdb dataset is publicly available on PhysioNet (Rodemund N, Koköfer A, Wernly B, Cozowicz C. "Salzburg Intensive Care database (SICdb), a freely accessible intensive care database" (version 1.0.5). PhysioNet. 2023. doi: <https://doi.org/10.13026/67ww-6m34>). However, contributor approved access is currently in place.

Declarations

Ethics approval and consent to participate

This study was approved by the State Ethic Commission of Salzburg, Austria (Approval Number: EK Nr: 1115/2021). Given the sole use of de-identified data, written informed consent was not required, in accordance with institutional and ethical guidelines.

Consent for publication

Not applicable, as this manuscript does not contain any individual person's data in any form (including individual details, images, or videos).

Competing interests

The authors declare no competing interests.

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