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Long-term survival after on-pump coronary artery bypass grafting in patients with coronary artery disease in Taiwan

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A B S T R A C T

The study analyzed the long-term survival of 1,482 eligible patients with coronary artery disease who received on-pump coronary artery bypass grafting (ONCAB) between 1997 and 2003 in Taiwan. The cumulative all-cause death rate over 23 years was 21.9%, while the cumulative cardiovascular-specific death (CVD) rate was 2.09%. Patients aged ≥ 70 years had a significantly higher incidence rate ratio (IRR) (IRR, 2.183, 95% confidence interval [CI], 1.742–2.731), but the lower cumulative incidence rate ratio (CIRR) (CIRR, 0.634, 95% CI, 0.524–0.767) for all-cause deaths than those aged < 70 years. There was no significant difference for IRR and CIRR of CVD between 2 groups. Overall survival was influenced by hypertension (hazard ratio [HR], 1.412, 95% CI, 1.104–1.806), dyslipidemia (HR, 1.890, 95% CI, 1.506–2.372), and previous stroke (HR, 0.525, 95% CI, 0.391–0.705) in all patients. Our results suggest that ONCAB may be a viable option for older patients.

Introduction

Due to demographic changes, Taiwan is expected to become a "super-aged society" by 2026, resulting in a higher burden of ischemic heart disease (IHD). IHD has a significant impact on mortality and disability worldwide, and has become an important public health issue since 2000 [1]. This social dilemma is not unique to Taiwan, and if left untreated, it could exacerbate the burden of our already strained healthcare systems.

According to statistics from the Taiwan Ministry of Health and Welfare, the average healthy life expectancy (HALE), representing the number of years lived in full health, was 71.67 years between 2007 and 2016. The gap between HALE and life expectancy in terms of disability-adjusted life years (DALYs) has steadily risen over the past decade due to population aging and IHD, which could intensify existing trends and widening the gap in Taiwan. However, the majority of extra years of life among Taiwanese people were spent in poor health and this data does not take into account trends in the types and severity of diseases over time (Supplementary Figure 5).

As we know, older patients with coronary artery disease (CAD), who typically have a longlist of comorbidities, make coronary artery bypass grafting (CABG) much more challenging. Many short- to mid-term trials have proven that CABG is not contraindicated for seniors, but inconsistent results were reported regarding the mid- to long-term survival of the older population [2–6]. In the current study, we evaluated the long-term survival of the older population with CAD receiving on-pump CABG (ONCAB) in Taiwan and tried to provide evidence of optimized strategies for our people.

Methods

Study design, setting, and population

This is a retrospective, single-center cohort study that involved patients who underwent elective, urgent, and emergency CABG between 1997 and 2003. Patients with incomplete clinical data and those who underwent combined CABG and valve surgery were excluded. These patients were further classified into two groups: group 1, aged <70 years; and group 2, aged ≥70 years. The study design is summarized in the supplementary flowchart.

Data collection

To determine patients' eligibility, either the paper-based or electronic medical records from the health record systems (HIS) were reviewed using Sybase SQL server. Data collection included demographics such as age and gender, as well as ejection fraction, and the number of involved coronary arteries on presentation, total number of

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grafts, baseline comorbidities, smoking history, and alcohol use. All comorbidities were adjudicated based on the 9th version of the International Classification of Diseases (ICD-9).

All causes of death were recorded during the follow-up period with the final follow-up date was December 31, 2021. Three reliable and acceptable sources for the time of death were used, including the death certificates provided by the patients' families, the death records from the hospital, and clinical follow-up records by investigators. Overall survival (OS) was measured from the date of CAD diagnosis and receiving surgery until the time of death from any cause or the last well-documented follow-up visits. Patients lost at intermediate follow-ups were censored at their last follow-up visits with medical records or phone interviews.

Statistical analysis

Categorical variables were summarized as numbers and percentages, and the Chi-Square test was used to determine statistical significance. Ejection fraction, the number of involved coronary arteries on presentation, and total number of grafts were divided into subgroups for multivariate analysis.

To test the difference between the two study groups and assess the impact of clinical variables, various methods were used, including the actuarial life-table method, the Kaplan-Meier methods with log rank test, Cox's proportional hazards model, incidence risk-ratio and cohort study risk-ratio analysis. The Nelson-Aalen analysis was also used to analyze how these two groups evolved over time.

Data were analyzed using IBM SPSS 22.0, and SATA 17.0. A P-value of less than 0.05 was considered statistically significant.

Results

Demographic and clinical characteristics

From January 1, 1997, to December 31, 2003, 1598 patients undergoing CABG were recruited for this study. After excluding patients with incomplete data, and those who received concomitant CABG (86 patients), a total of 1482 eligible patients (of whom 1157 were male) with a median age of 65 were enrolled. Baseline characteristics are provided in supplementary Table 1.

Comparison of post ONCAB-related all-cause and cardiovascular-specific deaths (CVD) between two groups

Among all eligible patients, out of the 325 deaths recorded, 9.5% were primarily due to CVD, while 90.5% were attributed to other causes. The cumulative all-cause death rate over 23 years was 21.9%, while the cumulative CVD rate was 2.09%. The median follow-up time was 142.5 months for group 1, and 90.5 months for group 2. Group 2 had a significantly higher incidence rate (IR) of all-cause deaths than group 1, with IRR of 2.183 (95% CI, 1.742–2.731, $p < 0.001$). The cumulative incidence rate ratio (CIRR) for all-cause deaths, which represents the ratio of the cumulative incidence rate of group 2 to that of group 1, was 0.634 (95% CI, 0.524–0.767, $p < 0.001$), indicating that group 2 has a lower cumulative incidence rate of all-cause deaths compared to group 1 (Supplementary Table 2.1). There was no significant difference for IRR and CIRR of CVD between 2 groups (Supplementary Table 2.2).

A comprehensive analysis of long-term survival and correlations following ONCAB

The cumulative survival rates in all eligible patients were 98% at 5 years, 87% at 10 years, 68% at 15 years, and 59% at 20 years. The 15-year cumulative survival rate was 69% for males and 68% for females. The median survival time for all-cause deaths was 23 years, and the estimated median survival time for CVD deaths was not acquired as less than 5% of patients died from cardiovascular diseases after surgery. The Kaplan-Meier method was used to estimate overall and cardiovascular-specific survival between the two groups (Fig. 1). The former was strongly influenced by some risks identified in this study (hazard ratio [HR], 2.768, 95% confidence interval [CI], 2.215–3.459, $P < 0.001$), but the latter revealed no statistical significance (HR, 1.194, 95% CI, 0.527–2.702, $P = 0.671$). Patients with preadmitted reduced LVEF had the worst OS ($P = 0.006$ log-rank test). The overall mortality rate did not appear to be statistically influenced by the number of involved coronary arteries and grafting numbers ($P = 0.416$ vs $P = 0.814$, log-rank tests) (Supplementary Figure 1).

For OS, the Nelson-Aalen cumulative hazard curves between the two groups appear similar, and the values are close initially. However, an apparent rise is noticed in group 2 compared to group 1 at the fifth year (HR, 2.768, 95% CI, 2.215–3.459, $P < 0.001$). For cardiovascular-specific survival, the two curves are roughly parallel in the first 10 years and after 10 years a slightly increased slope is seen in group 2 compared to group 1, but without significance (HR, 0.981, 95% CI, 0.758–1.271, $P = 0.886$) (Full model results are available in Fig. 1 and Supplementary Figure 3, 4).

Multivariate cox regression analysis: influence of comorbidities on overall survival

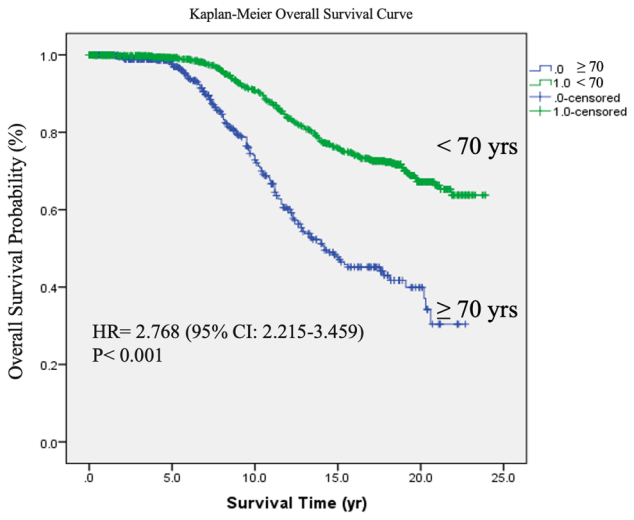
The forest plot displays the results of the multivariate Cox regression analysis, showing that in all eligible patients, OS was influenced by the presence of certain comorbidities, such as hypertension (HR, 1.412, 95% CI, 1.104–1.806, $P = 0.006$), dyslipidemia (HR, 1.890, 95% CI, 1.506–2.372, $P < 0.001$), and previous stroke (HR, 0.525, 95% CI, 0.391–0.705, $P < 0.001$) (Supplementary Figure 2).

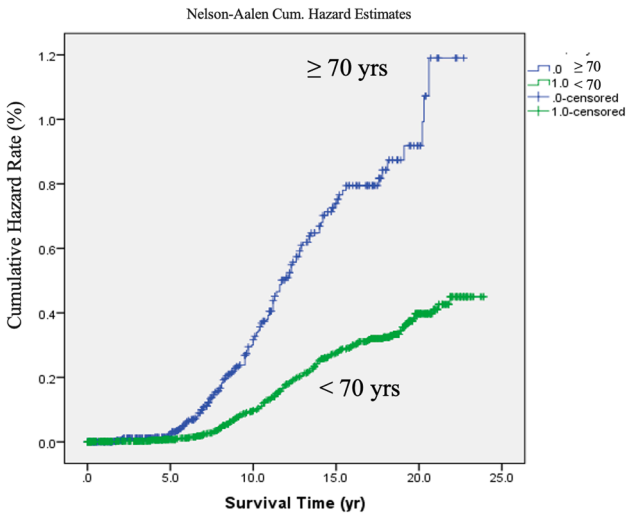
Discussion

Our study found that after 15 years, around 95% of ONCAB patients were still alive, with less than 5% experiencing cardiovascular-related mortality. The Kaplan-Meier analysis, risk-ratio estimation, and Nelson Aalen method all supported these findings, showing no significant difference in cardiovascular-specific survival between the two groups. Our results suggest that ONCAB prioritization in the older population excluding severe calcification and high-risk factors, may enable effective myocardial protection and complete coronary artery revascularization.

From a comprehensive analysis using risk-ratio estimation, Kaplan-Meier method, and Nelson-Aalen method, it is evident that CVD does not significantly contribute to the difference in post-operative mortality between the two groups. The higher incidence rate of all-cause deaths in groups 2 suggests a great likelihood of fatal events during the study period compared to group 1. However, the lower cumulative incidence rate of all-cause deaths in groups 2 indicates a lower probability of experiencing a fatal event at any given point. The Nelson-Aalen cumulative hazard curves further demonstrate that group 2 had a higher hazard than group 1, particularly after the fifth year post-ONCAB, indicating time-varying effects affecting survival probability. It is important to acknowledge that unmeasured factors, including differences in comorbidities, treatments, or lifestyle factors, may contribute to the observed variations between the two groups.

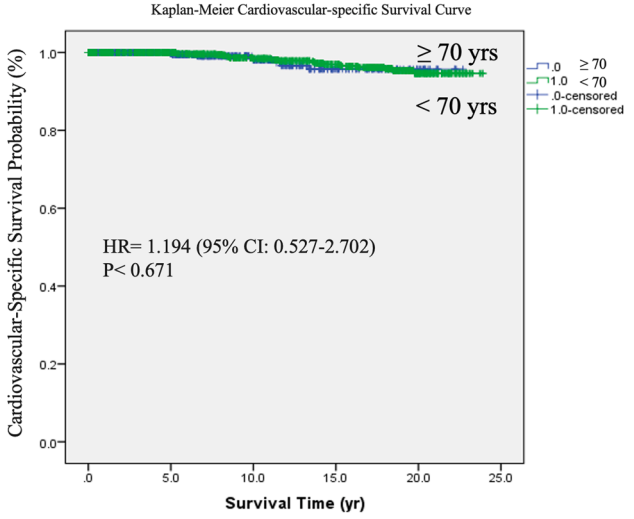
There may be contributing factors to the difference in mortality between the two groups that warrant consideration. In our study, we focused on several adjustable or non-adjustable factors. Among patients with CADs after ONCAB, low LVEF affected their survival time, while multi-vessel CAD and grafting number did not. We also examined the impact of comorbidities on long-term survival and found that hypertension, dyslipidemia, and previous stroke can be modified, treated, or controlled. These findings underscore the importance of taking into account various factors beyond age and CVD when making clinical decisions for patients with CAD before ONCAB.

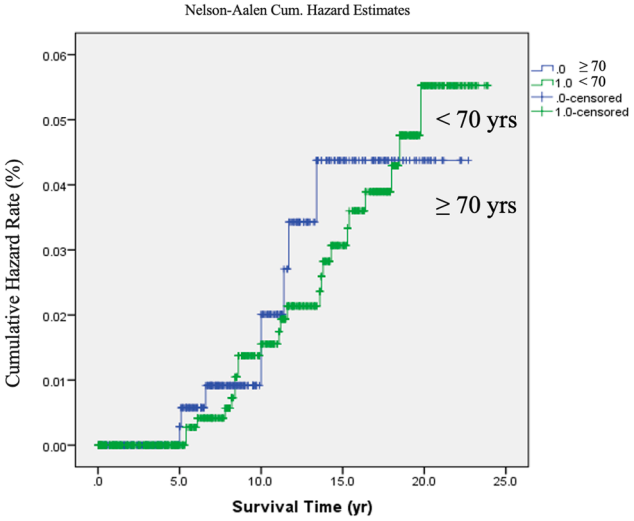




No. at risk (censored)

Yr	0	5	10	15	20
≥ 70	504 (0)	350 (8)	183 (79)	76 (135)	15 (143)
< 70	976 (0)	743 (6)	558 (62)	387 (147)	119 (176)





No. at risk (censored)

Yr	0	5	10	15	20
≥ 70	504 (0)	350 (1)	183 (4)	76 (8)	15 (8)
< 70	976 (0)	743 (0)	558 (10)	387 (17)	119 (23)

Fig. 1. The Kaplan-Meier & the Nelson-Aalen methods are used to assess overall survival (upper panels) and cardiovascular-specific survival (lower panels) differences between the two groups.

Our study has limitations that may affect the robustness of the results. It is a retrospective uni-center cohort study, which may introduce inherent misclassifications in data collection. Assumptions made based on the SYNTAX scores and the absence of a PCI comparison group are potential issues. Additionally, the impact of angina recurrence on survival times could not be quantified (20–30% patients experienced recurrence in our study). Lastly, we did not compare our study cohort with age- and sex- matched population data, potentially affecting the generalizability of our findings.

Conclusions

Our study demonstrated the long-term survival of the older population with CAD receiving ONCAB in Taiwan. Our findings suggest that older patients undergoing ONCAB may achieve a similar lifespan to the general population, which had an average life expectancy of 81.32 years in Taiwan in 2020 (78.1 years for males and 84.7 years for females). This implies that ONCAB may be a viable option for older patients. Further randomized controlled trials are needed to validate these results and explore the broader implications of our findings.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahr.2023.100152.

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