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Cangrelor in Patients with Percutaneous Coronary Intervention (PCI) after out-of-Hospital Cardiac Arrest (OHCA): A Propensity Score Matchig Analysis

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INTRODUCTION

Propensity Score Matching (PSM) is used in observational studies to measure the effect of a treatment by removing the bias of confounders, as randomisation is not possible. A multivariable logistic regression is performed to estimate the association of previously selected variables with the treatment administration, whilst the coefficients estimated from this regression are used to calculate a predicted probability of each patient receiving the treatment. Each patient in the treatment group is then matched to one or more patients in the untreated group based on the PS [1]. There are several ways to check whether PSM is successful or not: the two groups can be compared to confirm that there are no significant differences in covariate characteristics or the distribution graph of PS in both groups can be compared to ensure that they are similar. Once PSM is performed, unmatched patients are removed and analysis can be performed to test the treatment effect [1,2]. Out of Hospital Cardiac Arrest (OHCA) is defined as a sudden cessation of cardiac function with loss of consciousness and circulation occurred in out of hospital setting and acute coronary syndrome is the most common cause of OHCA. Emergent invasive coronary angiography (ICA) and percutaneous coronary intervention (PCI) has been shown to improve outcome in patients with ACS. Survivors of OHCA undergoing PCI are at higher risk of thrombotic and bleeding complications and cangrelor use has been shown to induce a faster, higher and more sustained inhibition of platelet aggregation function compared to all three P2Y12-inhibitors [3]. However, few data are available regarding OHCA victims.

AIM

The aim of this work is to apply PSM based analysis to investigate survival at hospital discharge of cangrelor use in OHCA survivors undergoing PCI.

METHODS

This is a multicentric, prospective, observational study involving all OHCA patients enrolled in the LombardiaCARe Registry from January 1, 2015, to December 31, 2022, who underwent PCI in seven centers in Lombardy region, Italy. Categorical variables were described as number and percentage and compared with the chi-squared test or Fisher exact test depending on the expected frequencies. Continuous variables were described as mean ± standard deviation and compared with the t-test or described as median and interquartile range (IQR) and compared with the Mann-Whitney test and according to their normal distribution tested with Shapiro Wilk test. All the variables that differed significantly between patients treated with cangrelor and patients in whom cangrelor was not administered were included in a multivariable logistic model for cangrelor administration. Model goodness of fit was assessed with Pearson test. The Area under the ROC Curve (AUC) was also computed. From the resulting coefficients PS was calculated. Patients were randomly matched according to the PS to generate random samples. The number of needed samples was established according to the convergence of the median chi-squared. The goodness of PSM was evaluated

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in term of balance of the baseline characteristics comparing the propensity distribution graph in the unmatched population and matched population and Kolmogorov-Smirnov test [2]. For each sample, considering only matched patients, chi-squared test and logistic regression were performed to test the association between cangrelor administration and patient in-hospital survival. The median chi-squared test and the overall odds ratio (OR) derived from each sample were taken into account to confirm the association between cangrelor administration and survival at discharge. Statistical analyses were performed with STATA 17. A two-sided p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 612 patients were admitted to the seven centres after OHCA and 414 (67.4%) underwent PCI. Among those patients 34 (8.2%) were treated with cangrelor. In the cangrelor group, 82.4% of patients were alive at discharge, compared to 65.3% in the no-cangrelor group (chi-square: 4.1; p-value: 0.04). A multivariable logistic regression model for the probability of receiving cangrelor was performed with all the significantly different variables between cangrelor and no-cangrelor group. (p-value: 0.001; PseudoR2: 0.2; AUC: 0.8). The model showed a good goodness of fit (Pearson chi2: 128.7; p-value: 0.8). Patients were randomly matched 25 times according to the PS to generate 25 random samples with 20 patients per each group, as indicated by the convergence of the median chi-squared (fig.1.a). Figure 1a demonstrates how the median Chi2s and ORs resulted from the Chi2 test and logistic regression for survival at discharge converge after 25 repetitions of PSM. The propensity distribution graph and Kolmogorov-Smirnov test showed a good PSM (p-value>0.05) in all 25 samples. The resulting ORs from the 25 samples with their 95% confidence interval are plotted in Figure 1b which shows that in all samples OR was OR>1 and an overall OR of 2.1 (95% CI 1.2-3.0) of survival at discharge, confirming the association between cangrelor administration and survival at discharge.

CONCLUSION

The multivariable logistic model for the association with cangrelor administration showed a good AUC and a good goodness of fit. The low number of patients treated with cangrelor prompted us to perform a random PSM to generate 25 random samples. The PSM was able to balance the baseline characteristics, making the two groups comparable. Moreover, repeating the PSM could help to achieve significant results in case of low numbers of patients and to overcome the limitation of PSM that leads to a reduction of the number of patients that can be included in the analysis due to the matching itself.

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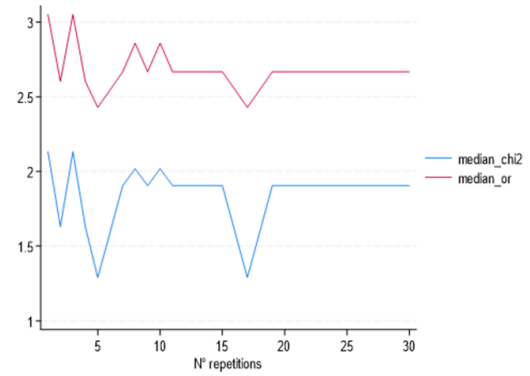
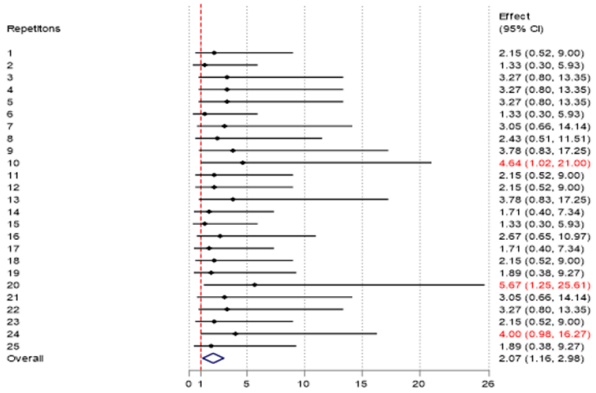


1A



1B

Fig.1: A: Median chi2 convergence graph B: Forest plot displaying the effect of cangrelor administration on the probability of survival at hospital discharge in all 25 random samples.

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