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EXTENDED ABSTRACT

Acute Kidney Injury after Coronary Artery Bypass Graft Surgery: The heterogeneity of the Available Real-World Data Through a Meta-analysis

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Introduction:

Meta-analysis is the method to pool data from studies that report the same event in a comparable sample and, thus, summarize information from different populations. However, data extraction is limited to the information provided in the included studies. Frequently, individual patient information is not available, hence, real world data access and data uniformization are limited.

To tackle high heterogeneity in a study-level meta-analysis, sensitivity analyses are recommended. Leave-one-out analysis is an option that evaluates the cumulative effect of each study by excluding one at a time, portraying its influence in the overall result [1].

Considering the lack of long-term data on postoperative acute kidney injury (AKI) in coronary artery bypass grafting surgery (CABG) patients, paired with the expected study heterogeneity, we intend to summarize evidence regarding its effect on early and long-term survival, evaluate heterogeneity and perform sensitivity analysis.

Methods:

Systematic searches were performed in MEDLINE and ISI Web of Science, restricted by date of publication (January 1960–April 2021). Inclusion criteria comprised observational studies reporting incidence of postoperative AKI in adult patients, submitted to isolated CABG with at least 1-year of follow-up and survival estimates.

Analyses were performed using Review Manager 5.4. and R environment. Random effects models were used to compute pooled HR and OR (95% CI), through generic inverse variance method and Mantel-Haenszel method. Generalized linear mixed-effects model and logit-transformed proportions of AKI were used for analysis of prevalence data. Heterogeneity was defined using I^2 statistics and was considered low (<49%), moderate (50-74%), or high (>75%) [2]. Between-study heterogeneity was studied using sensitivity analyses, namely, leave-one-out evaluations (metagen (meta R package)). Early and late survival were evaluated through this sensitivity analysis and were presented according to each study impact on both effect size estimates and observed I2. [3]

Results:

After screening 7369 titles and abstracts, 13 retrospective observational studies comprising 63209 patients were included, (N AKI=11366, N non-AKI=51843). AKI incidence ranged 0.6%-54% with a pooled incidence of 16%.

Postoperative AKI was associated with higher early mortality (OR (95%CI): 7.59 (3.18-18.15), $p<0.01$; $I^2=94\%$, $Chi^2=80.14$, $Tau^2=1.06$, $p<0.01$), but also with higher long-term mortality (HR (95%CI): 2.23 (1.83-2.70), $p<0.01$), with moderate heterogeneity ($I^2=74\%$, $Chi^2=42.92$, $Tau^2=0.08$, $p<0.01$).

In early mortality results, we observed a high effect on the leave-one-out analysis on I^2 (Figure 1) and on Baujat plot (Figure 2) by Ivert et al. [4] study which showed a relevant impact on heterogeneity. After removing this study, I^2 reduced to 0% and the pooled OR decreased and the 95% CI narrowed, (4.78 (3.74 - 6.09), $p<0.001$).

We observed the same for long-term mortality (Figures 3 and 4). The 2 most relevant studies for heterogeneity were Di Mauro et al. [5] and Lv et al. [6]. Although I^2 remained higher than 50% (I2=65%), after removing these two studies, the long-term survival pooled HR decreased and the 95% CI also narrowed, (1.98 (1.68-2.35), $p<0.001$).

Keywords:
Acute kidney injury; Coronary artery bypass; Data Analysis; Heterogeneity; Mortality; Meta-analysis; Population Characteristics; Research Design

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Conflict of interest:
The authors declare no conflict of interest.

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Figure 1 - Leave-one-out analysis for short-term mortality sorted by heterogeneity (I^2).

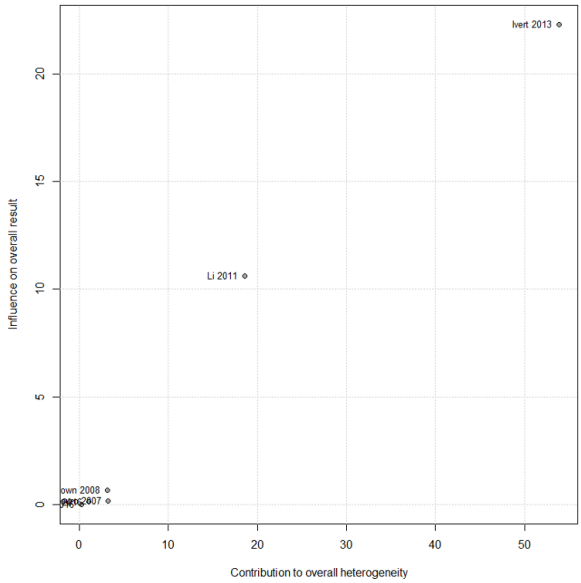

Figure 2 - Baujat plot showing the contribution of each study to the statistic for heterogeneity versus the influence of each study on short-term mortality.

Figure 3 - Leave-one-out analysis for long-term survival sorted by heterogeneity (I^2).

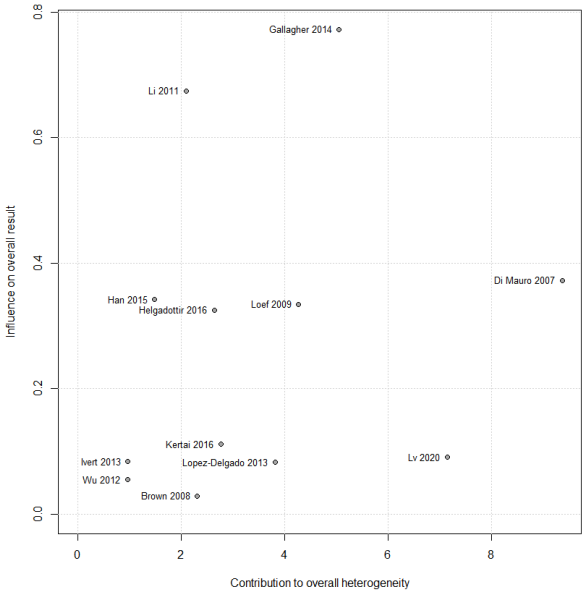

Figure 4 - Baujat plot showing the contribution of each study to the statistic for heterogeneity versus the influence of each study on long-term survival.

At meta-regression analyses, mean/median age, percentage of males, percentage of off-pump, mean/median and maximum follow-up were not found to significantly modify the effect of AKI on long-term mortality.

Discussion and Conclusion:

AKI is a frequent complication after isolated CABG surgery, being associated with higher long-term mortality.

The high heterogeneity found may be due to the different populations and variables' definitions. For instance, Ivert et al. [4] focused their analysis on patients who required postoperative dialysis, translating on a lower incidence of AKI, but also higher severity. Di Mauro et al. [7] defined AKI as an increase above 1 mg/dL or a postoperative value > 2 mg/dL according to preoperative renal function status, which differs from the most traditional criteria used by the other studies: increment of at least 0.3 mg/dL.

Leave-one-out analysis showed that one must pay attention to real-world data, since different variable definitions, namely: different AKI definitions and the samples included in each study, influence overall measures.

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