Bayesian Network Meta-Analysis of Upfront Surgery versus Neoadjuvant Therapy for Potentially Resectable Pancreatic Ductal Adenocarcinoma

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Aims: To compare upfront surgery and neoadjuvant treatment strategies for potentially resectable PDAC.

Methods: PubMed, MEDLINE, Embase, Cochrane Database and Cochrane Databases were searched for studies comparing neoadjuvant and upfront surgery. A Bayesian network meta-analysis was conducted using the Markov chain Monte Carlo method to better handle the heterogeneity of existing studies. Convergence was assessed using the Brooks-Gelman-Rubin method. In accordance with NICE guidelines inconsistency was measured by comparing deviance residuals and DIC statistic in fitted consistency and inconsistency models. Cochrane Collaboration's risk-of-bias, ROBINS-I and GRADE tools were used to assess the quality of included trials.

Results: 25 studies were included (n¼32,921). Aggregate rate (AR) of R0 was marginally higher with neoadjuvant therapy (0.7389 versus 0.7306, O.R 1.12, 95% CI 0.60-2.08). AR of 1,2,3,4 and 5-year survival were higher with neoadjuvant therapy (1-year survival: 0.8109 versus 0.6403, O.R: 2.12, 95% CI: 1.59-2.93; 2-year survival: 0.5135 versus 0.3002, O.R: 1.65 95%, CI: 1.16-2.34; 3-year survival: NAT 0.3151 versus 0.2147, O.R: 1.50, 95% CI: 1.10-2.04; 4-year survival: 0.2114 versus 0.1647 O.R: 1.57, 95% CI:0.80-2.99; 5-year survival: 0.2118 versus 0.1736, O.R: 1.65, 95% CI: 0.68-3.73). Multimodal treatment was the key determinant of optimal outcome.

Conclusion: Considering the flaws in the existing evidence neither treatment pathway is conclusively superior at population level analysis. Receipt of multimodal treatment at individual level within either pathway optimises outcomes. This study demonstrates the importance of developing statistical methods that better engage with system complexity and uncertainty to move towards more personalised predictive medicine to support decision-making.

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