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Thyroid

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Late Versus Early Administration of Radioiodine Therapy for Patients with Differentiated Thyroid Cancer: A Systematic Review and Meta-analysis

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Background: Radioiodine (RAI) therapy is an important adjuvant therapy for differentiated thyroid carcinoma (DTC) patients. Several studies have demonstrated the efficacy of RAI in reducing the risk of thyroid cancer recurrence and mortality; however, the ideal timing to initiate RAI after surgery is debatable. This systematic review and meta-analysis evaluates the risk of achieving excellent response and mortality when comparing late administration versus early administration of RAI in patients with DTC.

Methods: We searched Medline, Embase, Scopus, and Cochrane Database from inception to April 2021 to identify experimental and observational studies that evaluated the impact of different timings of RAI after surgery (<3 months vs. >3 months, <6 months vs. >6 months, <9 months vs. >9 months) on the risk of excellent response and thyroid-specific mortality in DTC patients with low, intermediate, and high risk of recurrence. We used random-effects model to pool dichotomous variables with odd ratios (OR) and their confidence intervals (95%CI). The risk of bias was evaluated using the Newcastle Ottawa Scale. PROSPERO Protocol ID CRD42021267036.

Results: We included 12 retrospective cohort studies with 34,833 patients. The majority of participants were female (78.00%) and the mean age ranged from 39.70 (\pm 3.40) to 51.60 (\pm 1.70) years. In patients with low-to-intermediate risk of recurrence, there were no differences in excellent response (OR 0.76, 95%CI: 0.34-1.68, I^2 : 78.00%, $n=1099$) and mortality risk (OR 1.00, 95%CI: 0.84-1.19, I^2 : 0.00%, $n=21450$) in the late group (>3 months) compared to the

early group (<3 months). The same outcomes were obtained for DTC patients who underwent RAI at 6 months (excellent response, OR 1.26, 95%CI: 0.94-1.69, I^2 : 0.00%, n=880) and at 9 months cut-offs (excellent response, OR 0.78, 95%CI: 0.32-1.91, I^2 : 0.00%, n=597; mortality, OR 1.28, 95%CI: 0.74-2.23, I^2 : 0.00%, n=327). Regarding DTC patients with high risk of recurrence, there were no differences in excellent response (OR 0.82, 95%CI: 0.61-1.11, I^2 : 0.00%, n=720) and mortality risk (OR 1.04, 95%CI: 0.74-1.47, I^2 : 62.50, n=10426) in the late group (>3 months) when compared to the early group (<3 months). Similarly for patients who underwent RAI at 6 months cut-off (excellent response, OR 1.04, 95%CI: 0.64-1.68, I^2 : 58.90%, n=72). However, mortality risk was higher in the late group (>6 months) when compared to the early group (<6 months) (OR 6.55, 95%CI: 2.92-14.67, I^2 : 0.00%, n=198). The risk of bias was considered moderate in 7 studies and high in 5. **Conclusions:** Low-to-moderate quality of evidence suggests increased mortality with delayed RAI (>6 months) in DTC patients with high risk of recurrence. The timing of RAI for other risk categories has little or no effect. Further experimental studies are needed to confirm these results and draw robust conclusions.

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