**DOACs or warfarin use in morbidly obese patients (BMI > 40 kg/m²) on anticoagulant therapy? : a systematic review and meta-analysis**

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**Introduction:** Current guidelines and consensus statements have advised against the use of direct oral anticoagulants (DOACs) for morbidly obese patients (BMI > 40 kg/m²), indicating warfarin as the first-line treatment.

**Purpose:** Our aim was to systematically review and examine the effectiveness and safety of DOACs compared to warfarin in patients with BMI > 40 kg/m² and atrial fibrillation (AF) or venous thromboembolism (VTE).

**Methods:** This study was conducted according to the PRISMA guidelines. We systematically searched PubMed, SCOPUS, and Cochrane databases from their inception to February 23, 2023, for studies comparing the effectiveness and safety of DOACs and Warfarin in extremely obese patients. The primary outcome was the incidence of the composite endpoint (stroke, systemic embolism, myocardial infarction, or all-cause mortality), ii) stroke/systemic embolism (SE) and, iii) VTE. Secondary endpoints referred to major and minor bleeding events.

**Results:** This meta-analysis comprised 16 studies and 114,999 morbidly obese patients with AF or VTE on oral anticoagulation therapy (48,937 on DOACs vs. 65,080 on Warfarin). The DOAC use was significantly associated with lower all-cause mortality and major bleeding rates compared to the warfarin group [risk ratio= 0.66; 95% confidence interval: 0.53, 0.81; p = 0.03; I² = 60%, RR: 0.78 (95% CI: 0.6-1.01, p <0.01, I² = 85%)]. Although the rates of composite endpoint, stroke/SE and VTE were lower in the DOAC group, no statistically significant difference was observed [RR: 0.88 (95% CI: 0.7-1.12, p <0.01, I² = 86%), RR: 0.92; (95% CI: 0.63-1.35, p <0.01, I² = 86%), RR: 0.72; (95% CI: 0.46-1.15, p <0.01, I² = 91%)], indicating no-superiority of Warfarin compared to DOAC use. The rates of minor bleeding events, hemorrhagic stroke and ischemic stroke were lower in the DOAC compared to warfarin groups [RR: 0.78 (95% CI: 0.56-1.10, p <0.01, I² = 80%), RR: 0.56 (95% CI: 0.26-1.21, p <0.01, I² = 86%), RR: 0.87; (95% CI: 0.6-1.24, p <0.01, I² = 81%)]. The same trend favoring DOACs over Warfarin in all the assessed endpoints was observed in the subgroup analysis when results adjusted for the anticoagulation indication (AF or VTE).

**Conclusions:** Our findings are of paramount importance indicating, firstly, the non-superiority of Warfarin compared to DOAC use, and secondly, a significantly better profile of DOACs in terms of safety and effectiveness in morbidly obese patients with BMI > 40 kg/m² in all the assessed endpoints. The findings may aid in the endeavor to enhance the upcoming recommendations for the management of this subgroup.