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"GLP-1Receptor Agonist Usage on Complications in Patients Undergoing Surgical Treatment of Endometrial Cancer"

Objective: Endometrial cancer (EC) is the most common gynecologic malignancy in the United States and the malignancy most strongly linked to obesity. Surgical intervention is the most common therapeutic intervention often in conjunction with systemic and radiation therapies. Due to recent widespread usage of GLP-1 Receptor Agonists (GLP-1RAs), there is a growing interest in understanding how they can be integrated into care plans for obese EC survivors. Our aim was to describe the incidence of surgical and postoperative complications in EC patients who have undergone surgical intervention for their EC, with a specific focus on rates of complications in those receiving GLP-1RAs at the time of surgery compared to those not using these medications.

Methods: Patients diagnosed with EC from 2019-2025 were identified. An IRB approved retrospective chart review was performed to GLP-1RA status, demographics, surgical details, Charleston Comorbidity Index (CCI), tumor histology and stage, molecular biomarkers, surgical approach, and complications. Chi-Square tests were used to compare categorical outcomes and two-sided t-tests were performed for continuous variables.

Results: Seventy-six women with EC were identified, most often presenting with grade 1 (n=25, 34.2%) or grade 2 (n=25, 34.2%) endometrioid adenocarcinomas and stage 1 disease (n=55, 65.8%). The predominant procedure was hysterectomy (n=60, 81.1%), but others had sampling or intrauterine device placements. Hysterectomy surgical approach was commonly robotic (n=47, 78.3%) but 11 (18.3%) were open. Fifteen patients (19.7%) were on GLP-1RAs perioperatively, often subcutaneous semaglutide injections (40%). GLP-1RA users within the database had a higher occurrence of stage 1 tumors (86.7% vs. 62.3%, p=0.195) and endometrioid adenocarcinomas (93.3% vs 72.1%, p=0.027) compared to non-users. The mean CCI score was 4.8 for non-users and 5.6 for users(p=0.210). All users had HER2 negative tumors, while non-users were HER2 negative 85.2% of the time (p=0.074). P53 signature trended towards more wildtype in GLP-1RA users than nonusers (93.3% vs 85.2%, p=0.077). Complications were overall uncommon and included 1 unplanned return to the OR, 1 prolonged stay,1 surgical site infection, and 2 unplanned readmissions. Complications were less common in the GLP-1RA user group than non-users, but this was not significant (0% vs 6.9%, p =0.2801). There were 2 mortalities within 30 days of surgery, both following endometrial sampling in medically frail patients who had advanced medical comorbidities.

Conclusions: No early indicators of significance were shown between GLP-1RA usage and complications, though overall rates of complications were quite low. A trend for an association between GLP-1RA use and p53 wildtype and HER2 negative tumors was observed, aligning with our understanding of obesity and these molecular subtypes of EC. A larger cohort is being collected and longer follow up is planned to better characterize interplay between GLP-1RA usage and EC prognosis.