

FASTING INSULIN AS A POTENTIAL MEDIATOR OF THE ADVERSE PROGNOSTIC EFFECT OF OBESITY IN LOCOREGIONAL BREAST CANCER. Goodwin PJ*, Ennis M, Madarnas Y, Pritchard KI, Trudeau ME, Hood N, Diamandis E. Marvella Koffler Breast Centre and Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto-Sunnybrook Regional Cancer Centre, Women's College Hospital, University of Toronto, 1284-600 University Avenue, Toronto, Ontario, Canada, M5G 1X5.

Obesity has been recognized as an adverse prognostic factor in locoregional breast cancer (LBC). Insulin, a known mitogen, was postulated to mediate this effect. Two related factors, IGF-1 and IGF-2, were also investigated.

An inception cohort of 535 women with LBC (T1-3, N0-1, M0) participated in the following measurements postoperatively: fasting blood collection, height (H), fasting weight (W) and Block Food Frequency Questionnaire. Tumor-related variables were abstracted from pathology reports. Subjects were followed prospectively for treatment, recurrence and death.

Mean age was 50.4 ± 9.7 years, mean body mass index ($BMI = W/H^2$) 25.4 ± 4.9 kg/m². Mean fasting insulin was 44.3 ± 31.0 pmol/l (normal range 13-161). Insulin was strongly correlated with BMI ($r = 0.59$, $p = 0$) but not with diet (total, fat, carbohydrate or protein calories, all $r < 0.10$). Insulin increased monotonically with each decade of age ($p < 0.001$).

Insulin was significantly associated with the following tumor-related variables: T stage ($p = 0.0006$, monotonic increments in postmenopausal women), N stage (41.9 ± 25.2 vs. 50.7 ± 41.1 in N0 vs. N1, $p = 0.02$, increasing monotonically with number of involved nodes: 41.9 ± 25.2 , 47.6 ± 36.1 , 50.1 ± 32.1 , 55.3 ± 52.6 in < 0 , 1, 2-3, ≥ 4 nodes respectively), T grade (increasing monotonically in grade 1, 2, 3: 39.9 ± 26.7 , 43.4 ± 33.6 , 48.7 ± 30.0 respectively, $p = 0.0001$). Insulin was not associated with estrogen or progesterone receptor status or with lymphatic invasion in the tumor ($p > 0.05$). Univariate survival curves suggest decreased 5-year disease-free and overall survival (DFS and OS) for insulin in the upper vs. lower quartile (OS 68 vs. 95%, DFS 65 vs. 90%).

IGF-1 and 2 were not significantly associated with BMI ($r < 0.20$) or any of these tumor-related variables (all $p > 0.05$).

These observations suggest insulin may mediate an adverse prognostic effect of obesity in LBC. Expanded survival data will be presented.