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55th Annual Meeting
May 31-June 4, 2019
McCormick Place
Chicago, IL

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55th
Annual Meeting of the American Society of Clinical Oncology
May 31-June 4, 2019

Chicago, Illinois

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1552 Poster Session (Board #46), Mon, 1:15 PM-4:15 PM

Insulin resistance measured by the triglyceride-glucose index and risk of obesity-related cancers: An epidemiological investigation in more than 500,000 individuals. *First Author: Josef Fritz, University of Colorado, Boulder, CO*

Background: The role of insulin resistance as a mediator in the association of body mass index (BMI) with site-specific cancer risk has, to our knowledge, never been systematically quantified. We aimed to determine to what extent insulin resistance measured as the logarithmized triglyceride glucose product (TyG index) mediates the effect of BMI on risk of obesity-related cancers. **Methods:** A total of 510,471 individuals from six European cohorts with a mean age of 43.1 years were included in the study. We fitted Cox models, adjusted for relevant confounders, to investigate associations of TyG index with ten common obesity-related cancer sites, and quantified the proportion of the effect of BMI mediated through TyG index. **Results:** During a median follow-up of 17.2 years, 16 052 individuals developed obesity-related cancers. TyG index was associated with the risk of cancers of the kidney (hazard ratio (HR) per one standard deviation increase 1.13, 95% confidence interval: 1.07-1.20), liver (1.13, 1.04-1.23), pancreas (1.12, 1.06-1.19), colon (1.07, 1.03-1.10), and rectum (1.09, 1.04-1.14). Substantial proportions of the effect of BMI were mediated by TyG index for cancers of the pancreas (42%), rectum (34%), and colon (20%); smaller proportions for kidney (15%) and liver (11%); none for endometrium, ovary and breast (postmenopausal). **Conclusions:** In this pooled cohort study including more than 500,000 individuals, insulin resistance measured as the logarithmized triglyceride glucose product significantly mediated the effect of overweight and obesity on risk of cancers of the kidney, liver, pancreas, colon, and rectum. In contrast, insulin resistance did not mediate the risk for cancers of the endometrium, ovary and breast. Our results confirm a promoting role of insulin resistance in the pathogenesis of gastrointestinal cancers. Although often claimed, insulin resistance does not appear to connect excess body weight with cancers of the female reproductive organs.

1553 Poster Session (Board #47), Mon, 1:15 PM-4:15 PM

Insurance disparity in the United States cancer survivors' smoking rates: A trend study from NHIS 2008-2017. *First Author: Yannan Zhao, Fudan University Shanghai Cancer Center, Shanghai, China*

Background: Smoking rates have been decreasing in the U.S over the last decade. Smoking cessation is a critical part of cancer treatment and survivorship care. However, little is known about the trend of smoking rates in U.S. cancer survivors and how it varied by individuals' insurance coverages. **Methods:** We conducted a retrospective study to evaluate the temporal trend of smoking rates using the National Health Interview Survey from 2008 through 2017. Adult cancer survivors (n = 20122) were included in the analysis. The outcomes were self-reported current smoking behavior. Insurance coverage was categorized into any private (age $\leq$65), other coverage (age $\leq$65), uninsured (age $\leq$65), Medicare + any private (age $>$ 65), and other coverage (age $>$ 65). We combined every two years data to improve statistical power in the subgroup analysis. Weighted analyses were performed with SAS 9.4 to account for the complex design. **Results:** The smoking rates in cancer survivors decreased from 18.4% in 2008 to 12.5% in 2017. However, the smoking rates varied remarkably by insurance status ($p < 0.001$). There was a decreasing trend of smoking rates in participants with any private (age $\leq$65) (17.3% in 2008/2009 to 12.0% in 2016/2017), Medicare + any private (age $>$ 65) (7.5% in 2008/2009 to 5.9% in 2016/2017), and other coverage (age $>$ 65) (13.2% in 2008/2009 to 9.2% in 2016/2017) whereas the current smoking rates remains high in cancer survivors with other coverage (age $\leq$65) (40.1% in 2008/2009 to 34.4% in 2016/2017) and uninsured (age $\leq$65) (43.4% in 2008/2009 to 43,1% in 2016/2017). **Conclusions:** Cancer survivors report less smoking behaviors over the last decade which is similar to the general population. However, the smoking rate remains dangerously high in non-elderly cancer survivors without any private insurance.

1554 Poster Session (Board #48), Mon, 1:15 PM-4:15 PM

Comorbidity and racial differences in risk of mortality of men with breast cancer. *First Author: Carol Parise, Sutter Institute for Medical Research, Sacramento, CA*

Background: Black men with breast cancer have more concomitant disease and worse survival than white men. Less is known about concomitant disease and survival in Hispanic and Asian/Pacific Islander (API) men with breast cancer. The purpose of this study was to compare differences in survival and risk of mortality of white, black, Hispanic, and Asian/Pacific Islander (API) men with breast cancer with increasing comorbidity. **Methods:** We identified 1,497 cases of first primary male invasive breast cancer from the California Cancer Registry 2000-2015 with a documented Charlson Comorbidity Index (CCI). The CCI is a weighted index based on the presence of certain comorbid conditions following a cancer diagnosis and weighted by the severity of these conditions. A score of 0 indicates no significant comorbidity and scores of 2 or more are interpreted as a high comorbidity burden. Bivariate associations between race and AJCC stage, tumor grade, estrogen receptor (ER) status, human epidermal growth factor 2 (HER2), and socioeconomic status (SES) were compared using the χ^2 Test of Independence. Kaplan Meier Survival analysis was used to compare unadjusted survival among the races. Cox Regression was used to assess risk of mortality for each race when adjusted for factors that had a statistically significant ($p < 0.10$) bivariate association with race/ethnicity. Analyses were conducted within each level of the CCI (0, 1, and 2 or more). **Results:** Among men with a CCI of 0 or 2, blacks had worse unadjusted survival than whites. There were no differences in survival for men with a CCI of 1. Stage, SES, ER, and type of surgery all had statistically significant bivariate associations with race/ethnicity. For men with a CCI of 0, Hispanics (HR = 0.367; 95% CI = 0.167, 0.801) and APIs (HR = 0.422; 95% CI = 0.189, 0.941) had a reduced risk of mortality when compared with whites. Black men had the same risk of mortality as white men. There were no differences in risk of mortality by race for men with a CCI of 1 or 2. **Conclusions:** Black men with breast cancer and no comorbidity have the same risk of mortality as white men while Hispanic and API men have lower risk of mortality. There are no racial disparities in adjusted risk of mortality in men with breast cancer with any concomitant disease.

1555 Poster Session (Board #49), Mon, 1:15 PM-4:15 PM

Burden of thrombocytopenia in adult cancer patients receiving chemotherapy. *First Author: Gerald A. Soff, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Thrombocytopenia is a common toxicity of chemotherapy, yet there are limited data on its occurrence in routine clinical practice. **Methods:** Using structured patient-level data from the Flatiron Health EHR-derived database, we assessed risk (3-month cumulative incidence) of chemotherapy-induced thrombocytopenia (CIT) in adult patients (2012-2017) based on platelet counts, overall and by each grade of CIT, cancer type, and chemotherapy regimen (Table); and the co-occurrence of other hematologic abnormalities. **Results:** Of 15,521 solid tumor patients who initiated chemotherapy, 13% had evidence of CIT within 3 months (platelet count $<100x10^9$/L), 4% had grade 3 (25 to $<50x10^9$/L) and 2% had grade 4 ($<25x10^9$/L) CIT. Of the solid tumors examined, incidence was highest in melanoma patients. In hematologic malignancies (N = 2,537), 3-month risk was even higher with nearly 30%, 16%, and 12% having any grade, grade 3 and 4 CIT, respectively; and the greatest risk being in multiple myeloma patients. Anthracycline-based regimens were associated with the highest risk of CIT (7% grade 3; 4% grade 4), followed by gemcitabine- and platinum-based regimens. Anemia often accompanied first evidence of CIT (49%); isolated thrombocytopenia occurred in 15%. **Conclusions:** This study provides a current snapshot of CIT risk in a large sample of adult patients undergoing chemotherapy in routine clinical practice, highlighting patients at highest risk for CIT and underscoring the complexity of managing cancer treatment.

Select chemotherapies and cancer types, N	3-month Cumulative Incidence % (95% CI): Overall	Grade 3	Grade 4
Gemcitabine, 1,662	15.8 (14.3, 17.4)	5.5 (4.5, 6.7)	2.5 (1.9, 3.2)
Platinum, 8,051	13.6 (13.0. 14.2)	4.3 (3.9, 4.7)	2.1 (1.8, 2.5)
Anthracycline, 1,972	16.4 (15.0, 18.0)	7.1 (6.0, 8.4)	3.6 (2.9, 4.4)
Taxane, 2,116	6.6 (5.7, 7.7)	2.0 (1.5, 2.5)	0.8 (0.5, 1.3)
Multiple Myeloma, 644	37.3 (34.2, 40.6)	23.5 (20.8, 26.6)	18.8 (16.4, 21.5)
Non-Hodgkin's Lymphoma, 1,321	24.4 (22.2, 26.7)	13.2 (11.5, 15.0)	9.1 (7.5, 11.0)
Melanoma, 58	21.4 (14.7, 31.2)	13.3 (6.8, 26.0)	5.0 (1.8, 14.1)
All Hematologic Malignancies, 2,537	28.2 (26.5, 30.0)	16.3 (14.8, 17.9)	12.4 (11.2, 13.8)
All Solid Tumors, 15,521	12.8 (12.3, 13.4)	4.2 (3.9, 4.6)	1.9 (1.7, 2.1)

Me-Can

Metabolic Syndrome and Cancer Project

http://me-can.se/

Insulin resistance measured by the triglyceride-glucose index and risk of obesity-related cancers: An epidemiological investigation in more than 500,000 individuals.

Josef Fritz[1,2], Tone Bjørge[3], Gabriele Nagel[4], Hans Concin[5], Jonas Manjer[6], Christel Häggström[7], Pär Stattin[8], Tanja Stocks[9], Hanno Ulmer[1]

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MEDICAL UNIVERSITY INNSBRUCK

Background

Excess body weight is a major risk factor for many cancer forms [1]. Three biological candidate mechanisms mediating the association of excess body weight with cancer risk were proposed [2,3].

i. Increased bioavailability of steroid hormones and alterations in sex hormone metabolism.
ii. Adipokine pathophysiology and systemic (subclinical) inflammation.
iii. Insulin resistance and bioavailability of insulin-like growth factor I (IGF1) (**Figure 1**).

The role of insulin resistance as a mediator in the association of body mass index (BMI) with site-specific cancer risk has, to our knowledge, never been systematically quantified. We aimed to determine to what extent insulin resistance, measured as the TyG index, mediates the effect of BMI on risk of obesity-related cancers, with a focus on gastrointestinal cancers and cancers of the female reproductive organs (gynecological cancers).

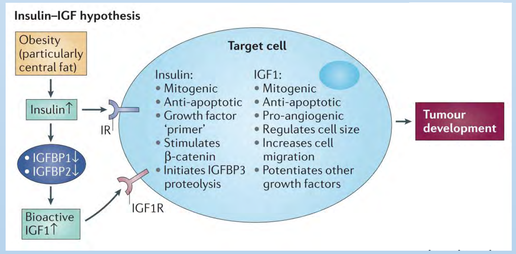

Figure 1. Biological mechanism of the insulin-IGF hypothesis. Adapted from [3].

TyG index: A novel measure for insulin resistance

- ✓ The logarithmized product of fasting levels of triglycerides and glucose (denoted TyG index) has been suggested to be a simple measure of insulin resistance [4].
- ✓ Both lipotoxicity and glucotoxicity play crucial roles in insulin resistance modulation and are reflected in the TyG index.
- ✓ The TyG index is highly correlated with the euglycemic-hyperinsulinemic clamp test, and has validity similar to the frequently used homeostatic model assessment (HOMA) insulin resistance (IR) index [5].
- ✓ Due to its easy availability and cost-effectiveness, the TyG index is a promising surrogate measure for insulin resistance in large-scale epidemiological studies.

Methods

A total of 510,471 individuals from six European cohorts (Me-Can project [6], http://me-can.se/, see graphic to the right) with a mean age of 43.1 years were included in the study. During a median follow-up of 17.2 years, 16,052 individuals developed obesity-related gastrointestinal and/or gynecologicial cancers.

We fitted Cox models, adjusted for relevant confounders, to investigate associations of TyG index with ten common obesity-related cancer sites, and quantified the proportion of the effect of BMI mediated through TyG index, using state-of-the-art mediation techniques according to VanderWeele [7].

Table 1. Baseline characteristics by quintiles of TyG index.

	TyG index Quintile 1 (N=102,521)	Quintile 2 (N=102,020)	Quintile 3 (N=101,851)	Quintile 4 (N=101,954)	Quintile 5 (N=102,125)
TyG index[1], mean (SD)	7.8 (0.2)	8.3 (0.1)	8.5 (0.1)	8.9 (0.1)	9.5 (0.4)
TyG index[1], range	<8.1	8.1 to 8.4	8.4 to 8.7	8.7 to 9.1	>9.1
BMI categories					
<18.5 kg/m2	3,859 (3.8%)	2,117 (2.1%)	1,359 (1.3%)	731 (0.7%)	289 (0.3%)
18.5 to 24.9 kg/m2	73,921 (72.1%)	62,974 (61.7%)	54,334 (53.3%)	43,441 (42.6%)	29,342 (28.7%)
25 to 29.9 kg/m2	21,268 (20.7%)	30,299 (29.7%)	36,304 (35.6%)	43,256 (42.4%)	49,769 (48.7%)
≥30.0 kg/m2	3,473 (3.4%)	6,630 (6.5%)	9,854 (9.7%)	14,526 (14.2%)	22,725 (22.3%)
Sex, male	33,153 (32.3%)	41,317 (40.5%)	49,640 (48.7%)	59,811 (58.7%)	74,047 (72.5%)
Age, yrs, mean (SD)	39.6 (11.0)	42.8 (10.7)	43.6 (10.7)	44.4 (10.2)	44.9 (9.4)

[1]: TyG index calculated as ln[triglycerides (mg/dl) x blood glucose (mg/dl)/2].

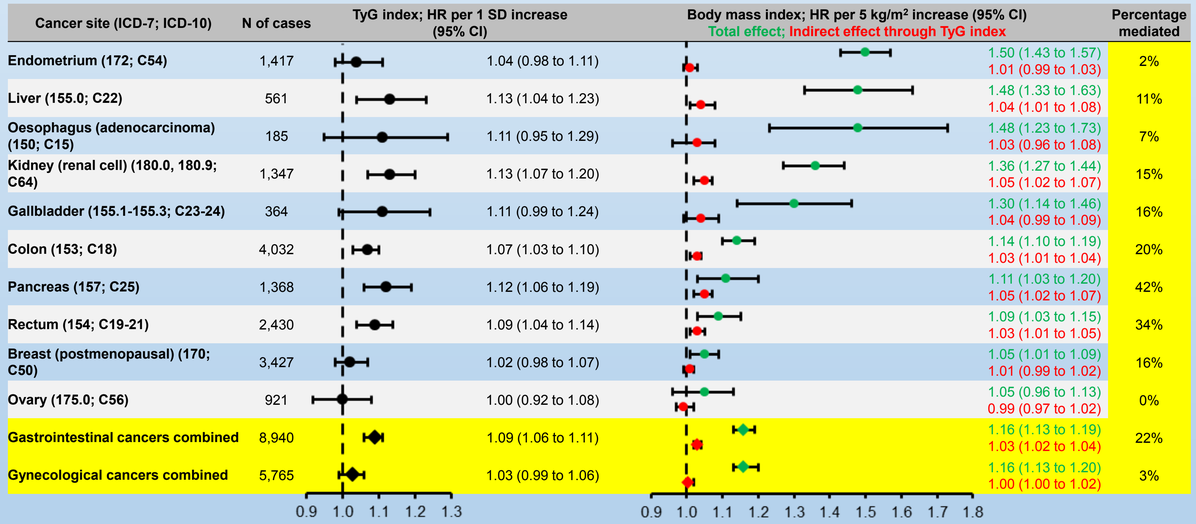

Figure 2. Effects of TyG index and BMI (total effect (in green) as well as indirect effect mediated through TyG index (in red)) on cancer risk, stratified by cancer site. All models adjusted for baseline age, sex, smoking status, fasting status, cohort, and decade of birth.

Results

Distribution of baseline characteristics of our population across TyG index quintiles are shown in **Table 1**.

TyG index was markedly stronger associated with the risk of gastrointestinal cancers than gynecological cancers. As expected, BMI was associated with an increased risk of all investigated cancer sites. Substantial proportions of the effect of BMI were mediated by TyG index for cancers of the pancreas, rectum, and colon; smaller proportions for kidney and liver; none for endometrium, ovary and breast (postmenopausal). **Figure 2** summarizes our findings separately for all ten different cancer sites, as well as gastrointestinal and gynecological cancers combined.

Further details will soon be published: Fritz J, Bjørge T, Nagel G, et al. The triglyceride-glucose index as a measure of insulin resistance and risk of obesity-related cancers. *Int J Epidemiol*. doi: 10.1093/ije/dyz053. [Epub ahead of print].

Conclusion and Key Messages

- ✓ In this pooled cohort study including more than 500,000 individuals, insulin resistance measured as the logarithmized triglyceride glucose product (TyG index) mediated part of the effect of overweight and obesity on risk of cancers of the pancreas, rectum, colon, kidney, and liver.
- ✓ In contrast, TyG index did not mediate the risk of cancers of the endometrium, ovary and breast.
- ✓ Our results confirm a promoting role of insulin resistance in the pathogenesis of gastrointestinal cancers.
- ✓ Although often claimed, our results provide limited evidence that insulin resistance connects excess body weight with risk of cancers of the female reproductive organs.

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