Renal cell carcinoma and body composition:

Results from a case-control study

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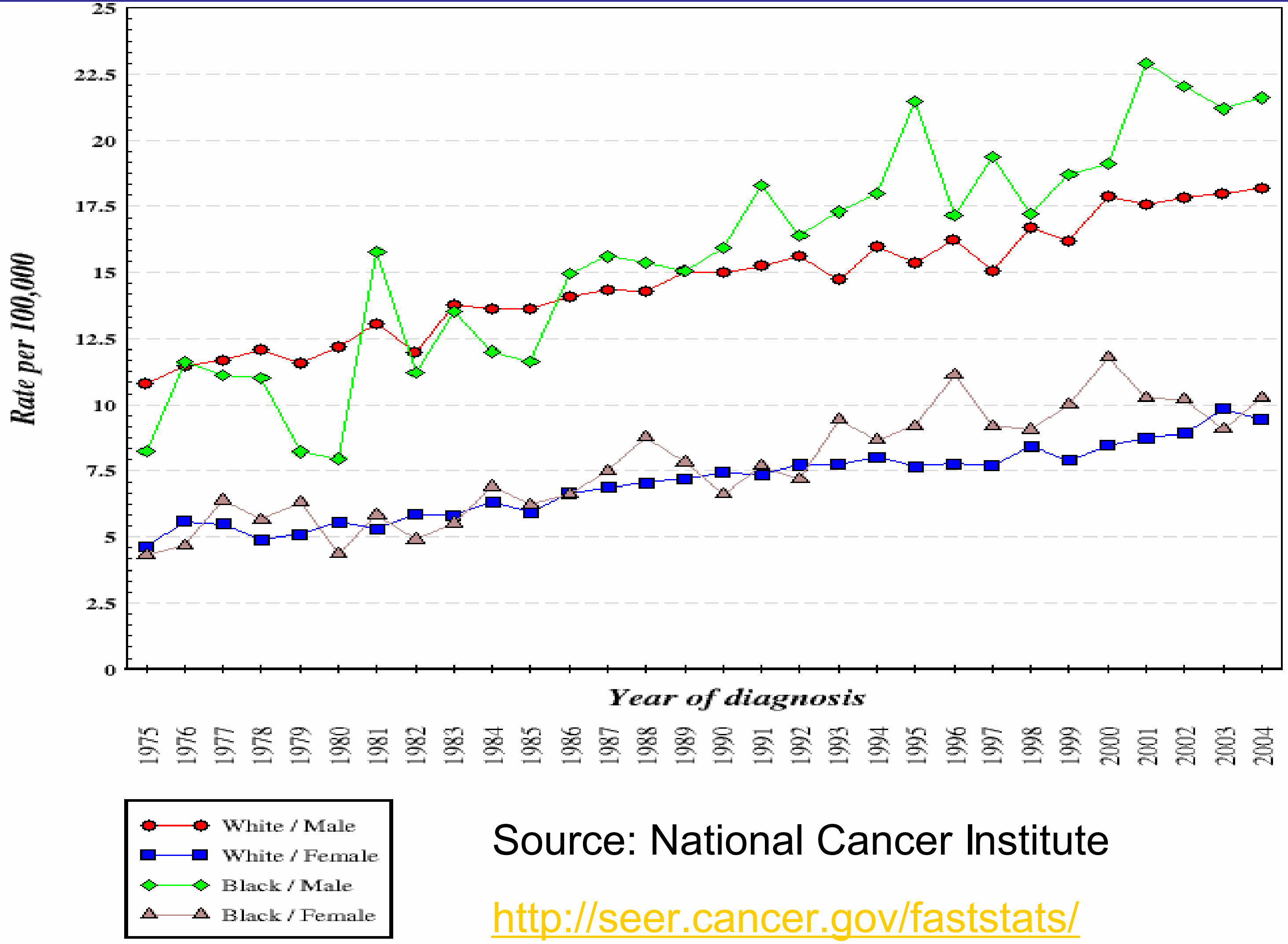
Background

- Kidney and renal pelvis cancers account for ~3.5% of all new cancer cases in the U.S.
  - 51,190 incident cases are estimated for 2007.
  - Renal cell carcinoma (RCC) accounts for 85%.
  - Incidence rates have doubled over the past 30 years.
    - Increases are greater among African-Americans than whites.
  - Known risk factors include smoking (OR ≈ 1.3), family history of RCC, dialysis, VHL disease.
    - Etiology is largely environmental.
    - The causes of RCC remain unknown, although studies have implicated hypertension, diabetes, occupational and dietary factors, and obesity.

Time Trend in Age-Adjusted Kidney/Renal Pelvis Cancer Incidence by Race and Gender U.S., SEER (9 areas), 1975-2004



Source: National Cancer Institute

http://seer.cancer.gov/faststats/

Background

- The prevalence of obesity (BMI $\geq$ 30) has risen at a corresponding rate over the past 40 years, to ~32% of the population in 2001-2004.
- The positive association between obesity and risk for RCC has been recognized by the IARC.
  - Meta-analysis reports a summary relative risk for RCC of 1.07 per unit increase in BMI (Bergström et al. 2001).
  - Findings are limited largely to BMI, which is an indirect indicator of body fat composition.
  - Findings on body fat distribution have been limited to waist-to-hip ratio (WHR).
  - While obesity may help explain secular trends in RCC, little is known regarding which aspects of obesity increase risk or the mechanisms by which obesity contributes to RCC etiology.

Study aims

- A population-based case-control study in Florida was conducted to:
  - Assess potential associations between RCC and various body composition factors (both self-report and anthropometric):
    - BMI : present; at age 20, 40, 60; maximum lifetime
    - Body fat composition (BF%)
    - Body fat distribution : WHR, 4-site skinfold thickness (abdomen, suprailiac, triceps, thigh)
  - Assess differences in the magnitude of RCC-obesity associations between African-Americans and whites.

Sampling methods

- Cases (N = 335): incident, histologically confirmed RCC
  - Identified through hospital records and the Florida Cancer Data System registry.
  - Diagnosed between Jan. 2000 and Dec. 2004.
  - Whites and African-Americans (AA) $\geq$ 20 years old.
  - Exclusions: tumors of the renal pelvis (TCC), cancer diagnosed in transplant kidney, out-of-state residence.
- Controls (N = 337): no history of RCC, from the general population
  - Identified using random-digit dialing and random sampling of telephone lists specific to African-American households.
  - Frequency-matched to cases by age (+/- 5 years), gender, and race.

Data collection methods

- In-person interviews using a structured questionnaire:
  - Medical, occupational and family histories
  - Lifetime smoking, beverage consumption, ETS exposure
  - Weight at age 20, 40, 60, and maximum lifetime

- Dietary profile using a food frequency questionnaire

- Body composition measurements at time of interview:
  - Height (cm) and weight (kg)
  - Circumference of waist (cm) and hips (cm)
  - Skinfold thickness (mm) at the abdomen, suprailiac crest, triceps, and thigh
  - BF% using foot-to-foot bioelectrical impedance (Tanita)

Data analysis methods

- Relative risks estimated by the odds ratio (OR) and 95% confidence interval (CI), using unconditional logistic regression.

- Body mass index (BMI) = weight (kg) / height (m^2)
  - Odds ratios estimated by WHO classification:
    - Healthy BMI = 18.5 – 24.9
    - Overweight BMI = 25.0 – 29.9
    - Obese BMI = 30.0 or greater

- Adjusted models controlled for: age, gender, race, education, smoking, daily caloric intake, daily fat intake.

- Tests for trend employed the Wald chi-square statistic, computed for continuous variables in adjusted models.

Study population

- Mean age at interview
  - Cases: 66 years
  - Controls: 62 years
  - T-test for difference, p = 0.001
- Gender
  - Women: Cases = 154 (46%) Controls = 161 (48%)
  - Men: Cases = 181 (54%) Controls = 176 (52%)
- Race
  - White: Cases = 262 (78%) Controls = 266 (79%)
  - AA: Cases = 73 (22%) Controls = 71 (21%)
- Diagnosis-to-study interval (cases)
  - Range: 0.4 years – 6.3 years
  - Mean: 3.1 years

Body mass index

BMI at time of interview

BMI	Cases		Controls		OR (95% CI)	Adjusted OR (95% CI)
	No.	**%**	**No.**	**%**		
18.5 - 24.9	50	15	70	21	1.00 (ref.)	1.00 (ref.)
25.0 - 29.9	118	35	123	37	1.34 (0.86 - 2.09)	1.19 (0.75 - 1.89)
≥ 30.0	166	50	136	41	1.71 (1.11 - 2.62)	1.58 (1.01 - 2.48)
Total	334		329			χ^2 trend p = 0.026

Maximum lifetime BMI

BMI	Cases		Controls		OR (95% CI)	Adjusted OR (95% CI)
	No.	**%**	**No.**	**%**		
18.5 - 24.9	21	6	41	12	1.00 (ref.)	1.00 (ref.)
25.0 - 29.9	90	27	102	30	1.72 (0.95 – 3.13)	1.45 (0.78 – 2.70)
≥ 30.0	223	67	192	57	2.27 (1.30 – 3.97)	1.95 (1.09 – 3.49)
Total						χ^2 trend p = 0.027

Body fat composition (BF%)

Body fat composition (BF%) quartiles, by gender

	Women					Men				
BF%	Cases		Controls		Adjusted OR (95% CI)	Cases		Controls		Adjusted OR (95% CI)
	No.	%	No.	%		No.	%	No.	%	
Q1	28	19	48	30	1.0 (ref.)	37	22	45	27	1.0 (ref.)
Q2	38	26	36	23	1.8 (0.9 – 3.5)	45	27	40	24	1.2 (0.7 – 2.4)
Q3	39	27	39	25	1.6 (0.8 – 3.1)	40	24	42	25	1.0 (0.6 – 2.0)
Q4	42	29	35	22	1.9 (1.0 – 3.7)	46	27	39	24	1.3 (0.7 – 2.5)
Total	147		158		Trend p=0.032	168		166		Trend p=0.042

- Body fat composition 40% or greater (dichotomous)
  - Reference: BF% < 40%
  - Odds ratio = 1.47 (1.05 – 2.05)
  - Adjusted odds ratio = 1.58 (1.05 – 2.37)
  - Trend p = 0.028

Body fat distribution - WHR

Waist-to-hip ratio quartiles, by gender

	Women					Men				
WHR	Cases		Controls		Adjusted OR (95% CI)	Cases		Controls		Adjusted OR (95% CI)
	No.	%	No.	%		No.	%	No.	%	
Q1	34	22	44	27	1.0 (ref.)	34	19	53	30	1.0 (ref.)
Q2	33	22	45	28	0.9 (0.5 – 1.8)	41	23	49	28	1.4 (0.7 – 2.6)
Q3	39	26	41	26	1.2 (0.6 – 2.3)	53	29	36	21	2.5 (1.3 – 4.8)
Q4	47	31	31	19	1.7 (0.8 – 3.4)	52	29	37	21	2.0 (1.0 – 3.9)
Total	153		161		Trend p=0.147	180		175		Trend p=0.052

- WHR $\geq$ 1.00 (dichotomous measure)
  - Reference: WHR < 1.00
  - Total sample: Adjusted OR = 1.46 (0.93 – 2.29)
  - Whites: Adjusted OR = 1.26 (0.76 – 2.11)
  - African-Americans: Adjusted OR = 3.49 (1.09 – 11.10)

Body fat distribution – skinfolds

Mean skinfold thickness values between cases and controls

	Cases	Controls	t-test	p value
Skinfold thickness (mm)				
Abdomen	30.20	28.78	-1.921	0.055
Suprailiac crest	23.38	21.69	-2.323	0.020
Triceps	23.77	22.99	-1.124	0.262
Thigh	27.86	26.08	-2.126	0.034
Core (Abdomen + Suprailiac)	53.69	50.46	-2.365	0.018
Total (all 4 sites)	105.62	99.39	-2.435	0.015

- Suprailiac crest skinfold, 4th quartile vs. 1st quartile
  - Women: Adjusted OR = 1.3 (0.7 – 2.5), Trend p = 0.426
  - Men: Adjusted OR = 2.1 (1.1 – 3.9), Trend p = 0.007

Discussion

- Obesity (BMI $\geq$ 30) increased RCC risk by 60% to 90%, whether assessed using present or maximum lifetime weight.
- Significant linear trends between BF% and RCC risk were observed for both genders.
- Measures of central adiposity (WHR, core skinfolds) significantly doubled RCC risk among men.

Discussion

- Body fat distribution results point toward metabolic syndrome as a potential mechanism:
  - Associated with central adiposity.
  - Resulting increases in insulin and IGF-1 promote cancer growth.
  - Renal cell tumor tissue has more IFG-1 binding sites than normal kidney tissue.
- Central adiposity (WHR) may contribute to a greater RCC risk increase among African-Americans than whites.
  - Studies of larger African-American samples are warranted to reproduce and clarify these findings.

References

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