Impact of glycemic parameters on breast cancer survival

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The presence of a causal link between glucose metabolism and breast cancer (BC) is highlighted by the epidemiological findings of a close relationship with type 2 diabetes (T2D), which translates into a 1.2 risk ratio for breast carcinogenesis. In addition, cancer patients with pre-existing T2D experience higher mortality than those without. However, an accurate assessment of the relationship between T2D and BC is often complicated by confounding factors (age, BMI, etc). Thus, results are often conflicting and the need for further studies has been highlighted in a recent joint AACE/ACE Consensus Statement.

Currently, our Centers are actively involved in the recruitment of ambulatory patients with primary or metastatic cancer, who are prospectively followed under the appropriate Institutional ethics approval, as part of a Clinical Database and Biobank project. Presently, a total of 1171 cancer patients provided informed consent to participate in the project, of which approximately 23% were diagnosed with BC.

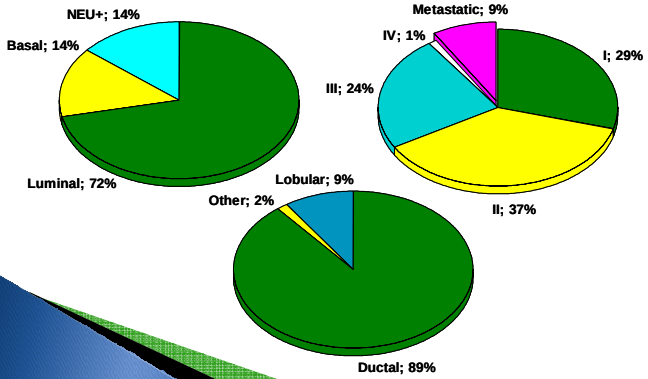
AIM of the study

Based on the hypothesis that impaired glucose metabolism might associate with survival outcomes independently of overt T2D, we sought to investigate the prognostic value of routinely used glycemic parameters in a prospective study of BC patients.

Patients and Methods

	*Cases (n=266)	Controls (n=133)	P level
Age (yrs)	58 ± 14	57 ± 13	NS
BMI	25.9 ± 5.1	25.0 ± 4.7	NS
Laboratory parameters at study entry			
Cholesterol (mg/dl)	211 ± 41	205 ± 42	NS
HDL(mg/dl)	56 ± 14	57 ± 12	NS
LDL (mg/dl)	130 ± 36	129 ± 36	NS
Glycaemia (mg/dl)	105 ± 33	85 ± 16	<0.0001
HbA1c (%)	5.7 ± 0.7	5.1 ± 0.5	<0.0001
Insulin (mIU/l)	9.6 (5.7 – 19.3)	6.6 (4.1 – 9.6)	0.0002
HOMA index	2.4 (1.2 – 5.5)	1.4 (0.9 – 2.0)	<0.0001

*8% meet the 2015 ADA criteria for T2D at time of breast cancer diagnosis



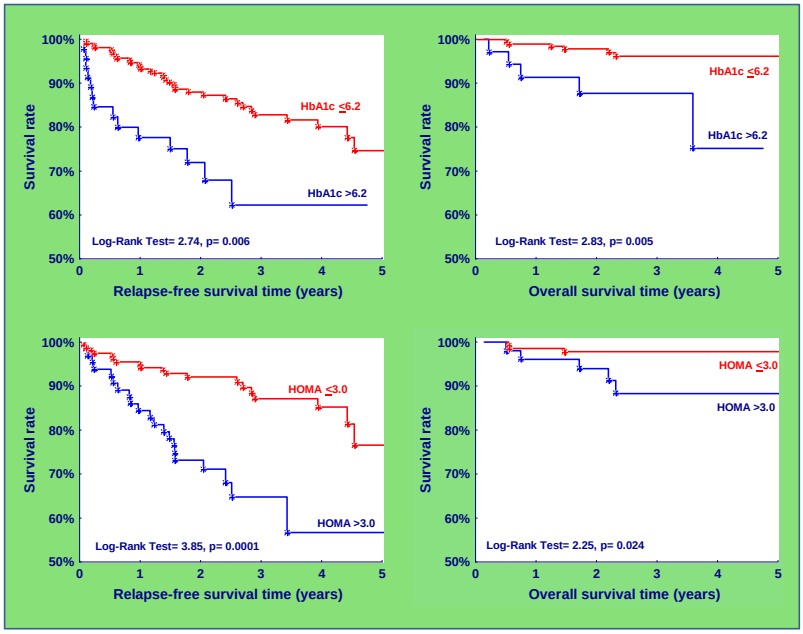
5-year follow-up was completed in all primary BC, with a median time of 2.5 years and a 14% recurrence rate.

Univariate COX proportional hazard analysis

	Relapse-free survival		Overall survival	
	HR (95%C.I.)	P value	HR (95%C.I.)	P value
Insulin	4.2 (1.9 – 8.9)	0.0002	10 (1.2 – 86)	0.035
HbA1c	2.5 (1.3 – 4.7)	0.004	4.8 (1.4 – 15)	0.010
HOMA Index	3.5 (1.9 – 6.6)	0.0001	5.4 (1.3 – 22)	0.020

Multivariate COX proportional hazard analysis

	Relapse-free survival		Overall survival	
Variable	HR (95%C.I.)	P value	HR (95%C.I.)	P value
Post-menopausal status	0.13 (0.04 – 0.50)	0.003	0.13 (0.03 – 0.66)	0.013
Histological diagnosis	0.54 (0.08 – 3.77)	0.536	0.88 (0.12 – 6 55)	0.905
Tumor stage	1.58 (0.73 – 3.43)	0.249	3.38 (1.26 – 9.09)	0.016
Estrogen receptors	0.15 (0.02 – 1.37)	0.092	1.09 (0.14 – 8.52)	0.933
Progesterone receptors	2.53 (0.23 – 27.8)	0.448	0.37 (0.04 – 3.40)	0.383
HER2 status	0.49 (0.11 – 2.27)	0.359	2.14 (0.54 – 8.48)	0.276
Ki67 proliferation index	5.07 (0.51 - 50.1)	0.164	2.27 (0.20 – 25.4)	0.504
HOMA Index	3.26 (0.82 - 13.0)	0.093	1.94 (0.39 – 9.49)	0.415
HbA1c	10.3 (2.0 - 52.8)	0.005	20.2 (2.93 – 139)	0.002



Conclusions

These results suggest that glucose metabolism contributes to survival outcomes in BC patients. This finding might be of relevance, especially in light of the positive impact of life style interventions in relation to BC risk. However, while the current evidence suggests that a significant proportion of BC cases could be prevented by lifestyle interventions, further studies are still needed to assess whether they may significantly reduce the risk of BC recurrence and mortality.

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