20W158

Does Possession Of The Z Or S Allele for α 1 anti-trypsin deficiency Influence Survival In BCLC Stage A/B Hepatocellular Carcinoma?

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Introduction

Alpha 1 antitrypsin (AAT) Z allele heterozygosity has been shown to increase the likelihood of developing hepatocellular carcinoma (HCC) (Zhou *et al.*, 2000). In both alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) it has been found to predispose to cirrhosis. The S allele too increases the risk in ALD (Strnad *et al.*, 2019). Given these cofactor roles, we questioned whether survival in HCC is affected by the presence of AAT deficient alleles. We tested this hypothesis on a cohort of patients treated for HCC at St Vincent's University Hospital.

Methods

Patients were recruited from a prospectively maintained HCC database in St Vincent's University Hospital. Patient consent for research was obtained prospectively in clinic when at first attendance. We included patients with Barcelona Clinic Liver Cancer(BCLC) stage A or B HCC. The survival of patients with Pi*Z/Pi*S was compared to the control group (PiMM) by generating a Kaplan Meier survival curve using SPSS® (2 tailed Log Rank test). Baseline demographic data was compared using Student t-test or Fishers exact test as appropriate.

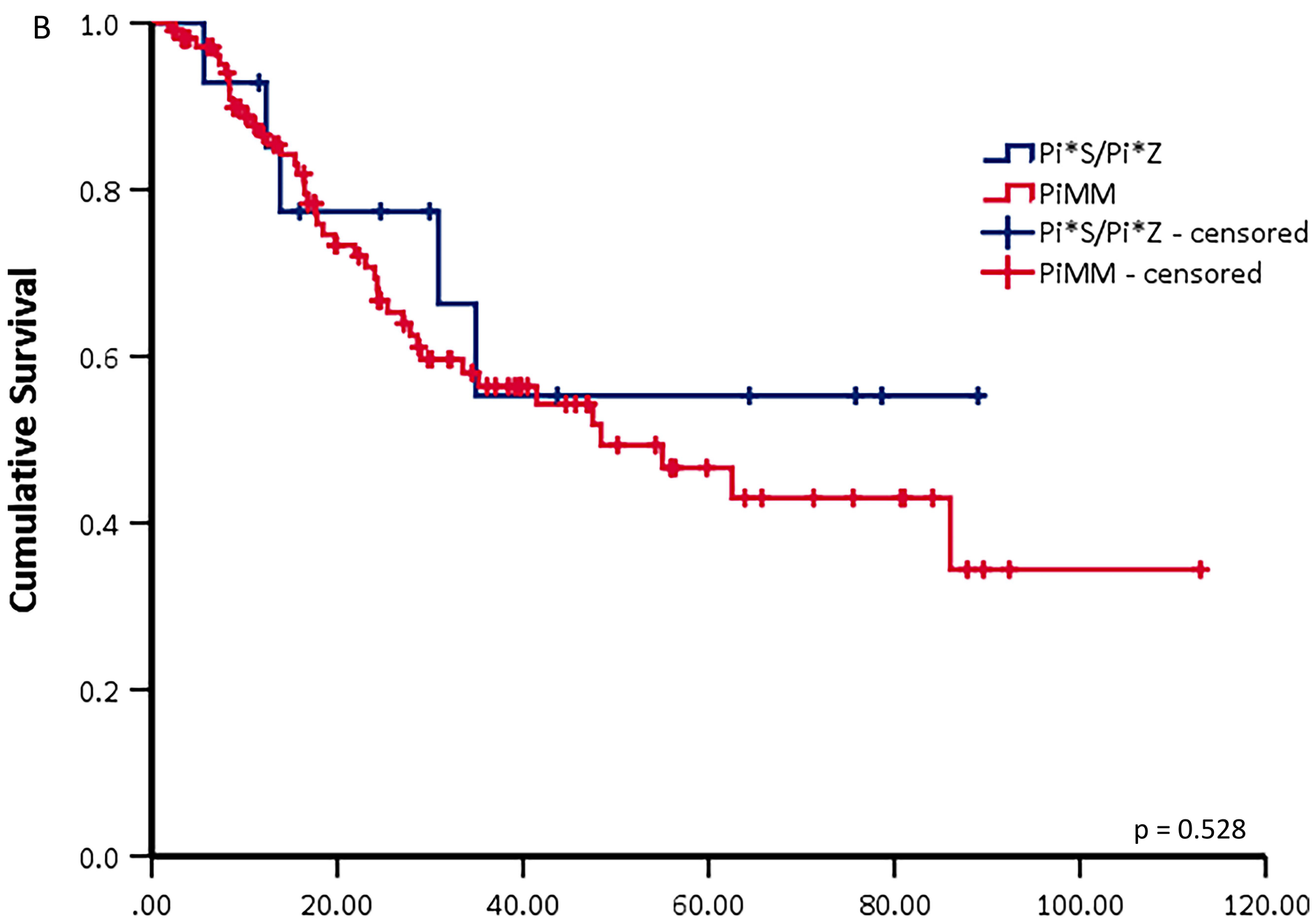
Results

There were 259 patients identified in the database with cirrhosis and BCLC stage A or B HCC. Only 122 of these patients had data available on AAT phenotype. Of these fourteen had either Pi*Z or Pi*S genotype (where * includes M, S, or Z allele, those with unidentifiable alleles were not included). One hundred eight patients had the wild type phenotype; the PiMM group. The groups' demographics were similar and statistically insignificant from one another with regards to age at diagnosis, sex, BCLC stage at diagnosis, levels of ALD/NAFLD, and rate of curative therapies (resection, radiofrequency ablation, or transplant)(see A). The mean follow up time for each group was 37.95 ± 26.99 months and 29.64 ± 24.44 months for Pi*S/Pi*Z and PiMM cohorts respectively. Kaplan Meier Survival analysis showed no significant difference between the groups (see B).

A

	PiMM	Pi*S/Pi*Z	Significance
Age at diagnosis	61.84 ± 7.93	63.80 ± 10.84	0.522 (t)
Sex (male)	93.52%	92.86%	0.634 (f)
BCLC A / B	77.78%/22.22%	71.43%/28.57%	0.735 (f)
ALD/NAFLD vs Other aetiologies	53.73%	50.00%	1.000 (f)
Curative Therapy	52.78%	57.14%	0.785 (f)

B



Number at risk (Number of events)							
Pi*S/Pi*Z	14	9	5	4	1	0	0
	(0)	(3)	(2)	(0)	(0)	(0)	(0)
PiMM	108	56	28	13	8	1	0
	(0)	(24)	(12)	(4)	(1)	(1)	(0)

Conclusions

Both the development of cirrhosis and HCC have been shown to be influenced by the presence of AAT alleles. Given such predilections, we felt it plausible to hypothesise and appropriate to investigate whether the possession of such alleles may also impact on patient outcome. Our results, however, do not show an impact on survival in BCLC stages A or B patients with HCC. Our study is limited by its retrospective nature, the cohort sizes, the inclusion of curative therapies, and the short follow up interval.

References

Strnad, P. *et al.* (2019) 'Heterozygous carriage of the alpha1-antitrypsin Pi∗Z variant increases the risk to develop liver cirrhosis', *Gut*. BMJ Publishing Group, 68(6), pp. 1099–1107. doi: 10.1136/gutjnl-2018-316228.

Zhou, H. *et al.* (2000) 'Is heterozygous alpha-1-antitrypsin deficiency type PiZ a risk factor for primary liver carcinoma?', *Cancer*. John Wiley & Sons, Ltd, 88(12), pp. 2668–2676. doi: 10.1002/1097-0142(20000615)88:12<2668::AID-CNCR4>3.0.CO;2-G.