Supplementary Table 1: Clinical characteristics of patients with positive and negative anti-HBs in the Hong Kong cohort

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristics | All | Anti-HBs positive | Anti-HBs negative | *P* |
| N | 233 | 144 | 89 |  |
| Age (years) | 51±11 | 52±11 | 50±11 | 0.44 |
| Male sex, n (%) | 126 (54.1) | 82 (56.9) | 44 (49.4) | 0.26 |
| Diabetes, n (%) | 141 (60.5) | 84 (58.3) | 57 (64.0) | 0.39 |
| Hypertension, n (%) | 131 (56.2) | 73 (50.7) | 58 (65.2) | 0.030 |
| Body weight (kg) | 76.9±16.1 | 76.0±16.2 | 78.4±16.0 | 0.27 |
| Body mass index (kg/m2) | 28.1±4.2 | 27.8±4.1 | 28.6±4.3 | 0.16 |
| Waist circumference (cm) | 95±14 | 95±14 | 96±14 | 0.39 |
| Men | 98±11 | 97±10 | 99±12 | 0.36 |
| Women | 92±16 | 91±17 | 93±15 | 0.53 |
| Total bilirubin (μmol/l) | 0.78±0.44 | 0.79±0.45 | 0.76±0.42 | 0.54 |
| Albumin (g/dl) | 4.5±0.4 | 4.6±0.3 | 4.5±0.4 | 0.080 |
| Alanine aminotransferase (IU/l) | 54 (36-80) | 54 (32-78) | 54 (40-89) | 0.21 |
| Aspartate aminotransferase (IU/l) | 29 (21-44) | 29 (20-44) | 30 (21-45) | 0.64 |
| Gamma-glutamyl transpeptidase (IU/l) | 55 (34-90) | 48 (32-90) | 61 (40-91) | 0.090 |
| Creatinine (μmol/l) | 0.86±0.25 | 0.86±0.18 | 0.86±0.33 | 0.94 |
| Fasting glucose (mmol/l) | 117±35 | 114±30 | 122±41 | 0.11 |
| Hemoglobin A1c (%) | 6.6±1.3 | 6.5±1.3 | 6.7±1.3 | 0.25 |
| Total cholesterol (mmol/l) | 189±44 | 191±48 | 187±36 | 0.55 |
| HDL-cholesterol (mmol/l) | 67±39 | 70±43 | 62±33 | 0.11 |
| LDL-cholesterol (mmol/l) | 111±33 | 112±33 | 110±33 | 0.67 |
| Triglycerides (mmol/l) | 115 (89-142) | 106 (89-124) | 124 (97-159) | 0.003 |
| Platelet count (x 109/l) | 231±77 | 234±70 | 226±88 | 0.47 |
| International normalized ratio | 1.02±0.59 | 0.99±0.11 | 1.07±0.94 | 0.30 |
| Anti-HBs titer (IU/l) | 123 (32-490) | 123 (32-490) | - | - |
| Anti-HBc positive, n (%) | 101 (43.3) | 90 (62.5) | 11 (12.4) | <0.001 |

Continuous variables are expressed as mean ± standard deviation or median (interquartile range).

Anti-HBc, anti-hepatitis B core antibody; anti-HBs, anti-hepatitis B surface antibody; HDL, high-density lipoprotein; LDL, low-density lipoprotein

Supplementary Table 2: Histological features of NAFLD patients with positive and negative anti-HBs

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | All | Anti-HBs positive | Anti-HBs negative | *P* |
| N | | 233 | 144 | 89 |  |
| Steatosis grade |  | 2 (1-2) | 2 (1-2) | 2 (1-3) | 0.11 |
| Lobular inflammation |  | 1 (0-1) | 1 (0-1) | 1 (1-1) | 0.18 |
| Hepatocyte ballooning |  | 1 (0-1) | 1 (0-1) | 1 (0-1) | 0.86 |
| Fibrosis stage |  | 1 (0-2) | 1 (0-2) | 1 (0-3) | 0.21 |
| NAFLD activity score |  | 3 (3-4) | 3 (3-4) | 4 (3-5) | 0.13 |
| NASH, n (%) | | 114 (48.9) | 68 (47.2) | 46 (51.7) | 0.51 |
| F2-4, n (%) | | 80 (34.3) | 47 (32.6) | 33 (37.1) | 0.49 |
| F4, n (%) | | 28 (12.0) | 17 (11.8) | 11 (12.4) | 0.90 |

Histological scores are expressed as both mean ± standard deviation and median (interquartile range), while comparisons are by the Mann-Whitney *U* test. NASH is defined as the presence of hepatic steatosis, lobular inflammation and hepatocyte ballooning.

Supplementary Table 3: Histological features of NAFLD patients with positive anti-HBc, stratified by anti-HBs status

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | All | Anti-HBs positive | Anti-HBs negative | *P* |
| N | | 101 | 90 | 11 |  |
| Steatosis grade |  | 2 (1-2) | 2 (1-2) | 1 (1-2) | 0.39 |
| Lobular inflammation |  | 1 (0-1) | 1 (0-1) | 1 (1-2) | 0.13 |
| Hepatocyte ballooning |  | 1 (0-1) | 1 (0-1) | 1 (0-1) | 0.70 |
| Fibrosis stage |  | 1 (0-3) | 1 (0-2) | 4 (1-4) | 0.021 |
| NAFLD activity score |  | 4 (3-4) | 4 (3-4) | 4 (3-5) | 0.52 |
| NASH, n (%) | | 53 (53) | 47 (52) | 6 (55) | >0.99 |
| F2-4, n (%) | | 41 (41) | 33 (37) | 8 (73) | 0.047 |
| F4, n (%) | | 18 (18) | 12 (13) | 6 (55) | 0.004 |

Histological scores are expressed as both mean ± standard deviation and median (interquartile range), while comparisons are by the Mann-Whitney *U* test. NASH is defined as the presence of hepatic steatosis, lobular inflammation and hepatocyte ballooning.

Supplementary Table 4: Liver-related events in 489 NAFLD patients

|  |  |  |  |
| --- | --- | --- | --- |
| Events | All | Anti-HBc positive | Anti-HBc negative |
| N | 489 | 170 | 319 |
| All liver-related events | 18 | 11 | 7 |
| Ascites | 4 | 2 | 2 |
| Varices | 11 | 6 | 5 |
| Variceal hemorrhage | 2 | 1 | 1 |
| Hepatic encephalopathy | 1 | 0 | 1 |
| Hepatocellular carcinoma | 4 | 4 | 0 |

The number of individual events added up to more than the total number because one patient could have more than one event.

Supplementary Table 5: Clinical characteristics of patients with NAFLD-related or cryptogenic hepatocellular carcinoma

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | All | Anti-HBc positive | Anti-HBc negative | *P* |
| N | 69 | 51 | 18 |  |
| Age (years) | 65±11 | 66±9 | 62±14 | 0.17 |
| Male sex, n (%) | 56 (81) | 44 (86) | 12 (67) | 0.067 |
| Diabetes, n (%) | 28 (41) | 22 (43) | 6 (33) | 0.47 |
| Hypertension, n (%) | 43 (62) | 32 (63) | 11 (61) | 0.90 |
| Body weight (kg) | 66.5±12.4 | 66.5±12.9 | 66.5±11.1 | >0.99 |
| Body mass index (kg/m2) | 24.7±3.8 | 24.5±3.9 | 25.4±3.7 | 0.40 |
| Alanine aminotransferase (IU/l) | 35 (25-56) | 36 (25-57) | 35 (27-48) | 0.80 |
| Alpha-fetoprotein (μg/l) | 61 (5-1265) | 63 (6-3146) | 49 (4-332) | 0.31 |
| F2-4 fibrosis, n (%)\* | 28 (48) | 22 (51) | 6 (38) | 0.35 |
| F4 fibrosis, n (%)\*† | 14 (24) | 10 (23) | 4 (25) | >0.99 |
| Child-Pugh class, A/B/C, n (%)† | 67 (97) / 2 (3) / 0 (0) | 49 (96) / 2 (4) / 0 (0) | 18 (100) / 0 (0) / 0 (0) | >0.99 |

Continuous variables are expressed as mean ± standard deviation or median (interquartile range).

\*In 59 patients who underwent liver resection (43 with positive anti-HBc and 16 with negative anti-HBc)

†Fisher exact test

Supplementary Figure 1: Distribution of fibrosis stage by region and ethnicity

