

# Association of AFP with Hepatocellular Carcinoma Subtypes

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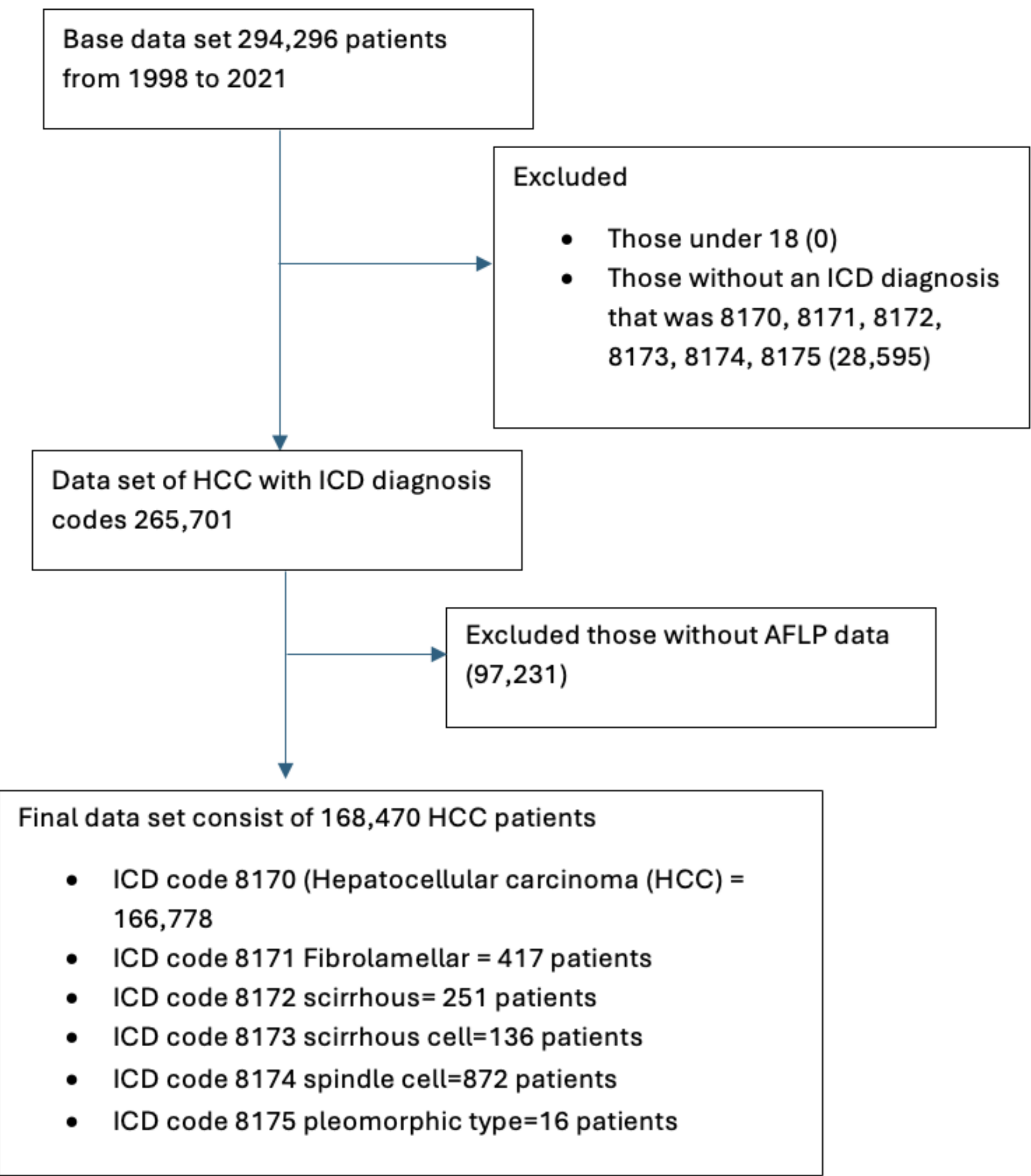
## INTRODUCTION

- HCC has many histological subtypes. Eight are currently recognized by the WHO classification<sup>1</sup>. This study will focus on the fibrolamellar, scirrhous, clear-cell, spindle-cell, and pleomorphic subtypes.
- An AFP level of >400-500 ng/mL is considered diagnostic for HCC<sup>2</sup>. AFP has also been correlated with prognosis in several studies<sup>3</sup>.
- The objective of this study was to characterize the relationship between AFP and the fibrolamellar, scirrhous, clear-cell, pleomorphic, and spindle subtypes of HCC.

## METHODS

- Retrospective cohort study examining the differences in and factors influencing mortality when AFP is elevated across the HCC subtypes.
- Utilized data from the National Cancer Database (NCDB).
- Hepatocellular subtypes were defined by the International Classification of Diseases for Oncology (ICD-O-3)<sup>4</sup>.
- Elevated AFP was defined as greater than or equal to 400 ng/mL.
- A 2-sample student t-test was used for continuous variables and a chi-square test was used for categorical variables. Survival was calculated using the Kaplan-Meier test.

Figure 1. Stepwise extraction process from acquirement of database to creation of final data set.



## RESULTS

Table 1: AFP levels in the histological subtypes

| AFP Lab Value            | Fibrolamellar* | Scirrhous  | Spindle-cell | Clear-cell* | Pleomorphic | HCC NOS      |
|--------------------------|----------------|------------|--------------|-------------|-------------|--------------|
| <20 ng/ml                | 286 (68.6)     | 106 (42.2) | 68 (50.0)    | 396 (45.4)  | <10         | 69369 (41.6) |
| ≥20 ng/ml and <400 ng/ml | 66 (15.8)      | 82 (32.7)  | 26 (19.1)    | 272 (31.2)  | <10         | 48403 (29.0) |
| ≥400 ng/ml (030+)        | 65 (15.6)      | 63 (25.1)  | 42 (30.9)    | 204 (23.4)  | <10         | 49006 (29.4) |
| Total                    | 417(100.0)     | 251 (100)  | 136 (100.0)  | 872 (100.0) | 16 (100)    | 166778 (100) |

\*P<0.05 when compared to HCC NOS

Table 2: Kaplan-Meier survival of the histological subtypes when stratified by AFP

|                                | Median Survival Months | P-Value |
|--------------------------------|------------------------|---------|
| Fibrolamellar + AFP <400 ng/mL | 39                     | <0.0001 |
| Fibrolamellar + AFP ≥400 ng/mL | 9.7                    |         |
| Scirrhous + AFP <400 ng/mL     | 3.8                    | <0.0001 |
| Scirrhous + AFP >400 ng/mL     | 24.2                   |         |
| Spindle-cell + AFP <400 ng/mL  | 3.2                    | 0.89    |
| Spindle-cell + AFP ≥400 ng/mL  | 3.7                    |         |
| Clear-cell + AFP <400 ng/mL    | 25.9                   | <0.0001 |
| Clear-cell + AFP >400 ng/mL    | 7.2                    |         |

\*All values made with 95% confidence interval

Table 3: Median survival months when stratified by stage of disease

| Stage 1                        | Survival Months | P-Value   | Stage 2                        | Survival Months | P-Value | Stage 3                        | Survival Months | P-Value  | Stage 4                        | Survival Months | P-Value   |
|--------------------------------|-----------------|-----------|--------------------------------|-----------------|---------|--------------------------------|-----------------|----------|--------------------------------|-----------------|-----------|
| Fibrolamellar + AFP <400 ng/mL | 76.7            | 0.3       | Fibrolamellar + AFP <400 ng/mL | 80.2            | 0.76    | Fibrolamellar + AFP <400 ng/mL | 32.3            | 0.0076 * | Fibrolamellar + AFP <400 ng/mL | 26.8            | <0.0001 * |
| Fibrolamellar +AFP ≥400 ng/mL  | 38.7            |           | Fibrolamellar +AFP ≥400 ng/mL  | 28.3            |         | Fibrolamellar +AFP ≥400 ng/mL  | 8.6             |          | Fibrolamellar +AFP ≥400 ng/mL  | 4.2             |           |
| Scirrhous + AFP <400 ng/mL     | 72.9            | <0.0001 * | Scirrhous + AFP <400 ng/mL     | 8.1             | 0.0082  | Scirrhous + AFP <400 ng/mL     | 96.9            | 0.29     | Scirrhous + AFP <400 ng/mL     | 96.9            | 0.29      |
| Scirrhous + AFP ≥400 ng/mL     | 11.5            |           | Scirrhous + AFP ≥400 ng/mL     | 2.6             |         | Scirrhous + AFP ≥400 ng/mL     | 66.7            |          | Scirrhous + AFP ≥400 ng/mL     | 66.7            |           |
| Spindle-cell + AFP <400 ng/mL  | 12              | 0.32      | Spindle-cell + AFP <400 ng/mL  | 17.2            | 0.59    | Spindle-cell + AFP <400 ng/mL  | 2.6             | 0.56     | Spindle-cell + AFP <400 ng/mL  | 2               | 0.89      |
| Spindle-cell + AFP ≥400 ng/mL  | 40              |           | Spindle-cell + AFP ≥400 ng/mL  | 9.4             |         | Spindle-cell + AFP ≥400 ng/mL  | 3.2             |          | Spindle-cell + AFP ≥400 ng/mL  | 1.97            |           |
| Clear-cell + AFP <400 ng/mL    | 47.6            | 0.026 *   | Clear-cell + AFP <400 ng/mL    | 34.6            | 0.29    | Clear-cell + AFP <400 ng/mL    | 10.6            | 0.25     | Clear-cell + AFP <400 ng/mL    | 8.51            | 0.0029 *  |
| Clear-cell + AFP ≥400 ng/mL L  | 30.7            |           | Clear-cell + AFP ≥400 ng/mL    | 22.6            |         | Clear-cell + AFP ≥400 ng/mL    | 7.5             |          | Clear-cell + AFP ≥400 ng/mL    | 2.279           |           |

## CONCLUSIONS

- Significant differences were observed between groups when AFP was elevated with spindle-cell having the highest percentage and fibrolamellar having the lowest<sup>5</sup>.
- Elevated AFP may be a marker of poorer prognosis for some subtypes. When AFP was elevated, median survival was significantly lower in fibrolamellar, scirrhous, and clear-cell. When stratified by stage and AFP, fibrolamellar and clear-cell continued to show a significant decrease in survival. AFP may act similarly, in some HCC subtypes, to CA 19-9 in pancreatic cancer<sup>6,7</sup>.

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