Appendix 1

Sample size estimation

The sample size was estimated based on tests for one ROC curve. The hypothesis of this study was that CTCs count can effectively distinguish whether HCC has metastasis, that is, the area under ROC curve (AUC) is greater than 0.5. According to the meta-analysis results of previous studies (32), the area under ROC curve of CTCs count was 0.93. When the value of significant level (α) was 0.05 (two-sided), the power of the test (1–β) value was 0.9, and the sample allocation ratio was 1:1, power analysis and sample size (PASS) 11.0 software estimated that at least 7 cases with metastasis and 7 cases without metastasis need to be recruited.

Since there might be many factors influencing HCC metastasis, the accuracy of the CTCs count in diagnosing HCC metastasis may be overestimated due to confounding factors when univariate analysis was performed. The AUC was set at 0.8 after a pre-test and expert panel discussion. All else equal, other parameters being unchanged, at least 17 patients with metastasis and 17 patients without metastasis should be recruited. Considering the influence of confounding factors and the principle of feasibility, we planed to double the sample size to ensure the inclusion of samples can obtain sufficient test efficacy. Furthermore, given that the shedding rate was set at 10%, more than 38 subjects need to be recruited in each group.

Finally, 104 subjects were actually enrolled in this study, of which 41 subjects developed metastasis and 63 subjects did not.

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Appendix 2

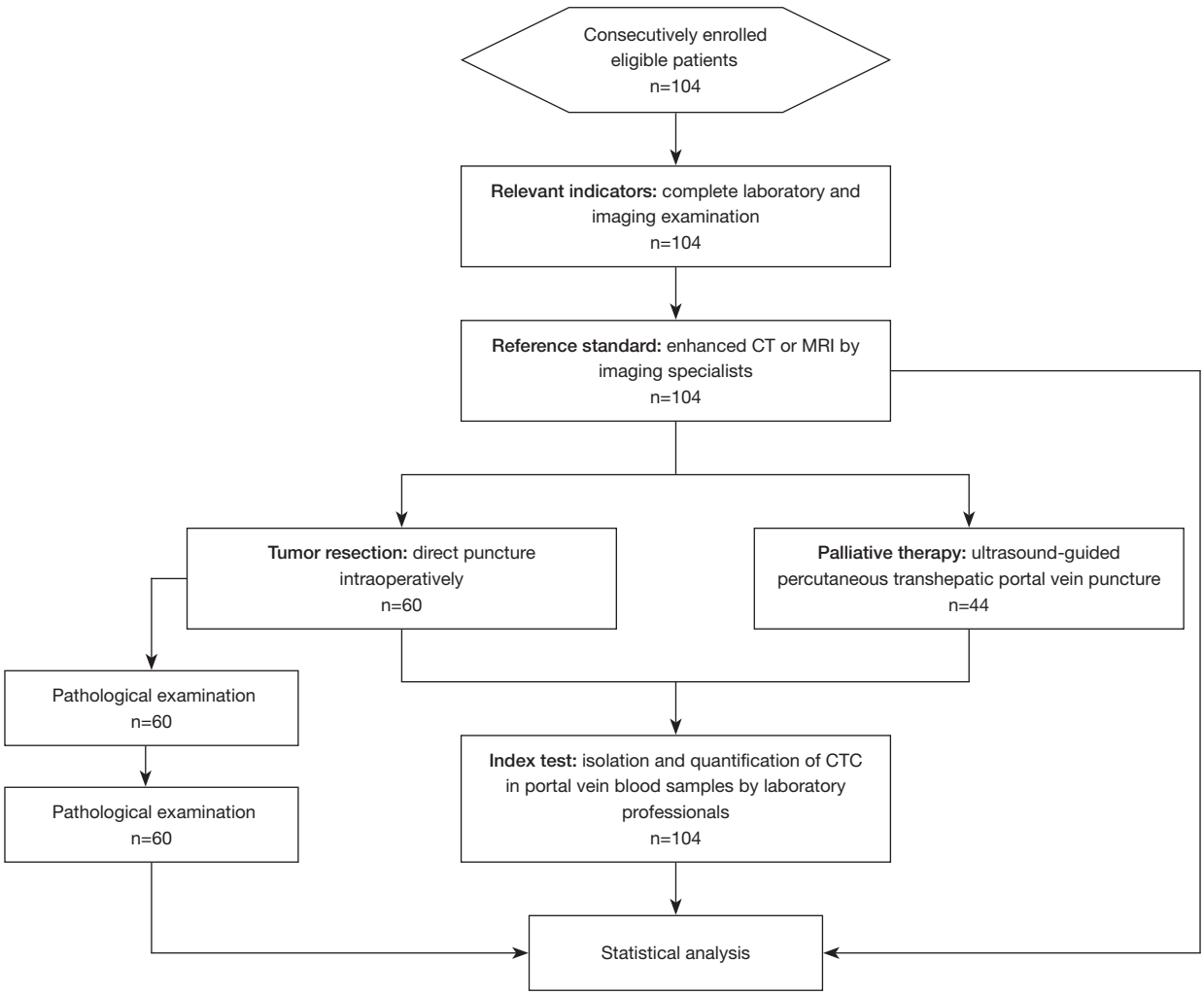

Figure S1 Research flow chart. CT, computed tomography; MRI, magnetic resonance imaging; CTC, circulating tumor cell.

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