

### Week 3 Discussion

Serum samples were drawn before surgery. No chemotherapy, radiotherapy, or targeted therapy was used prior to blood collection. For each patient, 8 mL of peripheral blood was obtained by venous puncture, followed by centrifugation at 3000 g for 10 min at 4°C. Cell-free serum was then stored at -80°C until RNA extraction. Control samples were obtained from 105 patients with benign liver disease (BLD) (75 patients with alcoholic liver disease and 30 patients with nonalcoholic fatty liver disease, all without hepatitis B infection) and 105 healthy volunteers (both age- and sex-matched).

The relative expression of serum UCA1 was detected and analyzed in each sample using reverse-transcription PCR.

Umehneku Chikere, C. M., Wilson, K., Graziadio, S., Vale, L., & Allen, A. J. (2018). Diagnostic test evaluation methodology: A systematic review of methods employed to evaluate diagnostic tests in the absence of gold standard – An update. *PLoS ONE*, 14(10). <https://doi.org/10.1371/journal.pone.0223832>

In the patient-control studies, the patients have to undergo the reference standard before the index test. In fact, people known to be affected by the target disease (“patients”) and people who are not affected (“controls”; i.e., healthy people or people with other diseases than the one we want to discriminate) are selected according to the results of the reference standard. Patient-control studies may be affected by spectrum bias which produces an overestimation of the index test accuracy.

<https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.26948>

This question is exemplified by a patient-control study on des-gamma carboxy-prothrombin (DCP) for the diagnosis of hepatocellular carcinoma (HCC).<sup>15</sup> Fifty-five patients with histologically proven HCC in liver cirrhosis (patients) and 53 patients with histologically proven liver cirrhosis (controls) were included. The mean serum concentration of DCP and the proportion of patients with a raised DCP value above the 125-mAU/mL cutoff were higher in patients with HCC (target disease). Another question is: are patients with a more advanced stage of the target disease more likely to have “abnormal” index test values than patients with a less severe target disease? To answer this question, a study has to include patients with different stages of the target disease. The study design is, again, the patient-control study (selection of groups of patients with a known stage of the disease).