Cromatografía líquida desnaturalizante de alto rendimiento (DHPLC)
Uso y utilidad en el genotipado masivo

Denaturing high performance liquid chromatography (DHPLC).
Use and utility in massive genotyping. Executive abstract
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Executive summary

Title: Denaturing high performance liquid chromatography (DHPLC).

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Background: Continuous and progressive advances on human genome’s knowledge as well as on its influences on health and disease have resulted in adding new genetic tests to clinical lab services. In addition to this, the growing request for genetic tests to be used has increased these labs’ activities. Part of their tasks is composed of detecting genetic variants which can specify, in some cases, DNA direct sequencing for an accurate diagnostics. Demand’s increase involves using techniques to screen genetic variants with the purpose of decreasing the number of cases subject to DNA sequencing.

Objectives: The overall objective is dealing with appropriateness and viability to implant DHPLC in clinical care areas to be used as genetic diagnostic tool. For that purpose, current diagnostic uses of DHPLC are further studied addressing its use in BRCA 1, BRCA 2, APC, RET oncogenes and genes related to mitochondrial encephalomyopathies. The analytical and clinical validity of such technique is being assessed; and the possible consequences of its introduction in care areas are being dealt with by guiding these data towards a subsequent economic assessment. The evaluation is consisting in considering incremental cost-effectiveness ratio (ICER) as result measure and in comparing different ICER of strategies to detect variants in the before mentioned genes.

Methodology: Systematic review of literature was run on MEDLINE and EMBASE reference data bases. There were retrieved the papers that dealt with the use of DHPLC in the analysis of BRCA 1, BRCA 2, APC, RET, oncogenes and genes related to mitochondrial diseases. The papers found were assessed following the advices on diagnostic tests by the STARD initiative, as well as recommendations by different institutions on assessing genetic tests. Afterwards the papers were selected, and those showing quantitative results were retrieved. The papers were assessed according to CASPe guidelines. For the economic assessment, a cost-effectiveness analysis was designed by using a deterministic model through a decision tree; the strategy followed for that purpose consisted in comparing screening with DHPLC as opposed to systematic sequencing (which was considered as gold-standard)
Results: Only 61 out of the 286 papers found were selected that met the inclusion criteria. Great variety was observed in the papers not only for diversity in the genes proposed in the present study but also for variety in designs and results. Most of them were transversal studies. A second selection got a total amount of 18 papers that, after being assessed with CASPe guidelines, achieved a score between 7 and 9 (out of 10). Generally speaking, DHPLC sensitivity observed were next to 100%. As regards to the economic assessment, the effectiveness measures used were the number of cases found and the number of effective cases (difference between cases found and cases lost). After extracting costs from literature, the incremental cost-effectiveness ratio (ICER) was considered as result measure. It was observed that ICER reached 278.13€ for the cases found and 139.07€ for effective cases when comparing DHPLC with sequencing. Sensitivity analysis showed in case the prevalence of the gene mutation samples overpassed 82% for effective cases and 85% for the cases found, the sequencing would be the strategy with the best ICER. However, if lower percentages were the case, DHPLC would maintain the best ICER.

Conclusions: DHPLC shows nowadays a wide range of utilities in the molecular study of a multiplicity of genes, including the analysis for clinical diagnostics. Among others, it is used to detect variants in BRCA 1, BRCA 2, APC, RET oncogenes and genes related to mitochondrial diseases. The possible introduction of DHPLC in clinical labs to screen genetic mutations sequences could influence the decrease in number of samples to which DNA sequencing will be performed. When such screening strategy is raised, there must be taken into account that DNA systematic sequence costs more (ICER: 278.13€) despite being more effective (which is mandatory as it is about the gold-standard).