Critical Look at Newborn Screening for Cystic Fibrosis

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Since September 2016, newborns in Germany are screened for Cystic Fibrosis (CF). Immunoreactive Trypsinogen (IRT) and Pancreatitis associated Protein (PAP) are used as biochemical markers in a three-stage process. Samples with an IRT result above the 99.9. percentile are reported as “screening positive” without any further tests (“failsafe” strategy). Samples with an elevated IRT concentration between the 99. and 99.9. percentile and an additional positive PAP result are analysed by PCR for the 31 most common mutations in the CFTR gene. According to the children’s guideline published in 2016, this screening algorithm was intended to be evaluated after 3 years, but this evaluation has not been performed yet.

Here, we present CF screening data from 777668 newborn dried blood samples, generated from March 2017 to June 2021 in Screening-Labor Hannover. In total, 783 cases were reported “screening positive” (0.10 %) and 140 of these were confirmed as CF later (17.9 %). 662 samples were found “screening positive” via “failsafe” strategy, of which 116 cases of CF were confirmed (17.5 %). Furthermore, 6191 newborns were tested positive for elevated IRT results between the 99. and 99.9. percentile. The following PAP analysis was positive in 23.2 % of those samples. The subsequent mutation analysis identified 18 of these 1437 newborns as either homozygous or compound heterozygous. All of those were confirmed as CF cases later. Additionally, 103 heterozygous newborns were reported as “screening positive”. In this cohort, only 6 cases of CF were confirmed (5.8 %).

The aim of the CF screening process is to identify as many newborns affected by CF as possible while minimising false positive results. However, the current algorithm results in a large number of false positive cases. In earlier and more recent publications, various approaches have already been described achieving better results with the same analytical tools. Our data point out that there is the potential to significantly improve the specificity of the CF screening process, especially in the “failsafe” cohort.