Exploring the Potential Yield of Prenatal Testing by Evaluating a Postnatal Population with Structural Abnormalities

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After identification of one or more structural abnormalities in a fetus, pregnant women are offered a host of different testing options to identify a possible genetic cause for the structural abnormality(ies). When considering what type of test to undertake, there is limited information on the diagnostic yield of the varying testing options. Some women may miss an opportunity to gain the information they are seeking or make a less informed decision when they choose a testing option after identification of a structural abnormality due to this lack of information. This study aimed to identify the potential diagnostic yield of all currently available prenatal testing options in the presence of a structural abnormality through a retrospective chart review of a postnatal population of infants with structural abnormalities. Of 791 patients with at least one structural abnormality, 691 patients underwent genetic testing and 222 had a genetic aberration that explained their phenotype. Chromosomal microarray had the highest potential diagnostic yield across the entire cohort and among individuals with multiple structural abnormalities, 26.8% (95% CI: 23.5 - 30.3) and 29.0% (95% CI: 25.3 - 33.3) respectively, which reached significance (p <0.001, p = 0.029) compared to all of the other prenatal screening and diagnostic options. In the isolated cohort, whole exome sequencing had a higher potential diagnostic yield of causative pathogenic aberrations, followed by chromosome microarray. Expanded non-invasive prenatal testing (NIPT with microdeletions and whole genome NIPT) had a higher potential yield than traditional NIPT. Whole genome NIPT also had a comparable yield as a karyotype, although this did not reach statistical significance. While interesting, it is important to consider the limited data available on expanded NIPT panels compared to the robust studies of traditional NIPT and how this might affect these results and post-test counseling regarding positive screening results. This study provides further evidence for the use of chromosomal microarray for the highest potential diagnostic yield in genetic testing after identification of one or more structural abnormalities.

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