NIPS for patients with high BMI: evaluating the impact of whole genome sequencing

Introduction

Fetal fraction (FF) is one of the many factors that influence the performance of noninvasive prenatal screening (NIPT). Lower FF is associated with early gestational age, a compromised placenta (e.g., from diabetes and certain aneuploides), and high body mass index (BMI). The most common of these is high BMI: patients with high BMI contain >20% of FF, leading to an increase in the performance of NIPT due to lower fetal nucleated cells in maternal serum. However, the most common risk factor for fetal aneuploidy, triploidy, and certain aneuploidies, and high BMI.

Study design

5,737 consecutive patients who provided their height and weight and received WGS-based NIPS were analyzed by stratifying into standard BMI classes. FF closely follows a beta distribution, allowing parameterization across classes (Figure 3). For each BMI group, the aggregate analytical sensitivity (Figure 1) was calculated by summing — over the range of FF values — the product of the analytical sensitivity for each FF window. The higher the class, the higher the frequency of low FF, but in all cases the analytical sensitivity for T21 is 99.8%, whereas for class III it is 95.4%.

Results

The distribution of FF over various classes of BMI demonstrates that a large proportion of women with high BMI would have a FF ≤4%, which would result in a high test failure rate if FF alone were used as a cut-off. This is in contrast with similarly high test failure rates seen by others.10

As BMI increases, NIPS sensitivity drops due to decreased FF, leading to lower “no-call” rates. While the majority of studies have focused on normal BMI patients, few studies have evaluated the impact of high BMI.11,12

Conclusion

Due to their systematically lower FF, high-BMI patients are subjected to a higher “no-call” rate for NIPS compared to standard maternal serum screening (92.9%). As such, high-BMI patients could be subjected to a lower-quality of care. However, we demonstrate that NIPS alone is a superior option for high-BMI patients when using methods that maintain high sensitivity at low FF such as whole-genome sequencing, allowing providers to offer the same high level of care to all of their patients, regardless of body habitus.

REFERENCES


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