Diagnostic Value of Brain MRI in Newborns with Congenital Cytomegalovirus Infection

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Background

The association between brain abnormalities and congenital cytomegalovirus (cCMV) infection has been well known for decades, however the prevalence of these lesions remains unknown. While some abnormalities, like cortical malformations, seem strong predictors of poor neurological outcome, the prognostic role of others, such as white matter lesions is not well known. Neonatal MRI has shown a lot of potential in addition to ultrasound for detecting cCMV-related lesions, however, at present, there still is no consensus for its role in screening infected newborns, especially in the absence of clinical symptoms.

Aim

The aim of this thesis was to investigate the value of brain MRI in newborns with cCMV, with an emphasis on white matter lesions.

Results

The aim of the thesis was subdivided into 4 four research questions, which were presented in four publications:

1. Spectrum and frequency of abnormalities detected on neonatal brain MRI

First, we investigated the spectrum and frequency of abnormalities detected on brain MRI in a large cohort of 196 infected newborns. The overall frequency of brain abnormalities was 39%. Although brain abnormalities were significantly more frequent in clinically symptomatic patients (77 versus 33% , P<0.01), they were still detected in over 30% of otherwise asymptomatic patients (Figure 1). White matter lesions were the most commonly detected abnormality, followed by subependymal cysts and ventricular dilatation. Many patients showed multiple concomitant lesions. White matter lesions frequently occurred in association with other types of abnormalities (such as cortical malformations), however in 45%, they were noted as an isolated abnormality (1) .

2. Qualitative scoring of the white matter and correlation with clinical outcome

In the second, prospective study, we developed a qualitative scoring system for visually assessing the white matter on neonatal brain MRI. The white matter was subdivided into normal, abnormal and doubtful white matter. The clinical implications of isolated white matter lesions were investigated in terms of hearing, motor and cognitive development.

Qualitative grading of the white matter was feasible, with good interobserver agreement (Cohen's weighted kappa value 0.79). Isolated white matter abnormalities were associated with neonatal hearing loss (odds ratio (OR) 20, P <0.05) and mildly lower motor scores (OR 8, P < 0.05) at clinical follow-up. A tendency towards impaired cognitive development was seen (OR 5, P = 0.07). Patients with discrete or doubtful white matter did not show worse outcome, compared to children with a normal MRI (2).

3. Quantitative scoring of the white matter and correlation with clinical outcome

The third, retrospective study, investigated if quantitative measurement of the white matter on neonatal brain MRI, by means of apparent diffusion coefficient (ADC) values, could be used to predict clinical outcome. ADC was measured in 255 newborns. White matter ADC was significantly higher in patients with neonatal hearing loss and with cognitive and motor impairments during follow-up (P <0.05) . White matter ADC, in combination with other qualitative imaging variables, allowed a fairly good distinction between children with and without clinical impairments, with receiver operating characteristics area under the curve (ROC AUC) ranging between 0.73 and 0.89 (Figure 2) (3).

4. Systematic review of current literature on the value of MRI in congenital cytomegalovirus

Finally, we performed a systematic review of the current literature on the value of MRI in children with cCMV. Twenty articles were included in the review. MRI can detect a wide range of brain abnormalities, both in pre- and postnatal setting, both in clinically

symptomatic and asymptomatic patients. MRI can be a helpful tool in the prediction of clinical impairments and seems complementary to ultrasound (4).

Conclusion

MRI can detect a wide range of brain abnormalities, both in clinically symptomatic and asymptomatic patients. MRI, with qualitative and quantitative interpretation of the white matter, can be a helpful tool in predicting clinical impairments and guiding therapy. Although further research is necessary, MRI should be considered in all cCMV-infected newborns.

FIGURE 1: Bar chart displaying the rate of abnormal brain MRI, in cilincally symptomatic and asymptomatic newborns with cCMV.

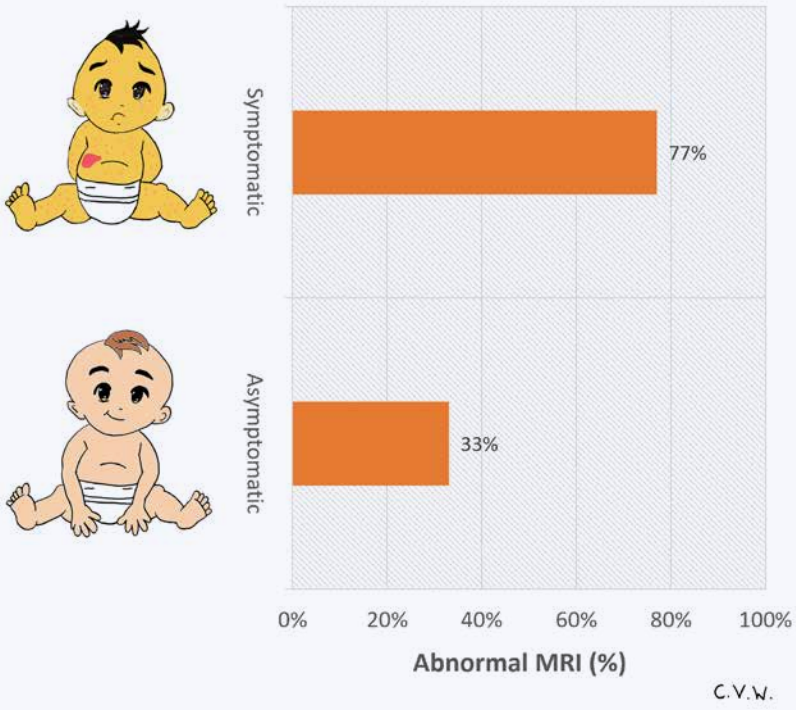
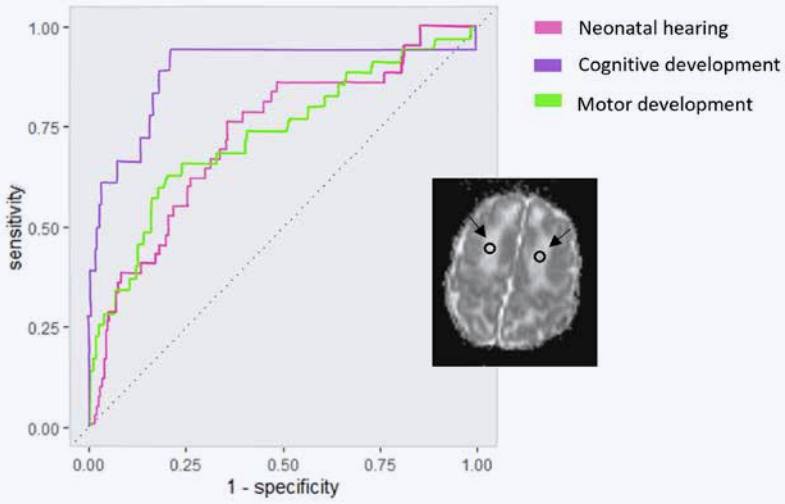


FIGURE 2: Receiver Operating Characteristics curves of the final models using white matter ADC for predicting clinical outcome.



REFERENCES

1. Vande Walle C, Keymeulen A, Schiettecatte E, Acke F, Dhooge I, Smets K, et al. Brain MRI findings in newborns with congenital cytomegalovirus infection: results from a large cohort study. Eur Radiol. 2021;31(10):8001-10.
2. Vande Walle C, Keymeulen A, Oostra A, Schiettecatte E, Dhooge IJ, Smets K, et al. Implications of isolated white matter abnormalities on neonatal MRI in congenital CMV infection: a prospective single-centre study. BMJ Paediatr Open. 2023;7(1).
3. Vande Walle C, Keymeulen A, Oostra A, Schiettecatte E, Dhooge I, Smets K, et al. Apparent diffusion coefficient values of the white matter in magnetic resonance imaging of the neonatal brain may help predict outcome in congenital cytomegalovirus infection. Pediatr Radiol. 2024;54(2):337-46.
4. Vande Walle C, Maris F, Schiettecatte E, Herregods N. The value of magnetic resonance imaging in congenital cytomegalovirus infection: a systematic review. Pediatr Radiol. 2024;54(13):2157-74.