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Letter to the Editor

Letter to the Editor regarding "Can early cranioplasty reduce the incidence of hydrocephalus after decompressive craniectomy? A meta-analysis"

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To the editor

Nasi and Dobran published a meta-analysis considering the influence of timing of cranioplasty (CP) after decompressive craniectomy on post CP hydrocephalus.[9] They reported no significant difference in postoperative hydrocephalus rate between early (i.e., within 3 months) and late (i.e., after 3 months) CP, but they did find a significantly lower incidence of hydrocephalus after early CP when only studies specifically reporting on patients with traumatic brain injury (TBI) were included in the meta-analysis. Therefore, they concluded that early CP after decompressive craniectomy performed in TBI patients is associated with a lower incidence of hydrocephalus. In our opinion, the methodology of this study raises several questions, precluding the conclusions drawn by the authors.

Assessing the methodological quality

To report a meta-analysis accurately and completely, it is important to use a guideline, such as PRISMA.[7] Although Nasi and Dobran describe the use of PRISMA in their methods section, many checklist items are not mentioned in their paper (e.g., presenting full search strategy, performance of study selection and data extraction in duplicate, list of excluded studies (with reasons), risk of bias assessment, and heterogeneity discussion). According to the AMSTAR checklist, the study would qualify as a critically low quality review.[15]

Heterogeneity among studies

The authors' finding that early CP in TBI patients is associated with a lower incidence of post CP hydrocephalus is based on significant heterogeneity (I^2 = 85%). This considerable variation in results, in particular inconsistency in the direction of effect, makes it questionable to quote the intervention effect.[5] Moreover, the authors performed a fixed effect meta-analysis, which ignores heterogeneity. A random effects meta-analysis, although not a substitute for a thorough investigation of heterogeneity, would have been more appropriate since it incorporates heterogeneity among studies.[5] When performing such random effects meta-analysis, early CP in TBI patients is *not* associated with a lower incidence of hydrocephalus [Figure 1].[3,10,12,14]

Importantly, the included cohort study performed by Nasi *et al*. reported a hydrocephalus rate of 48% in the late CP group versus 5% when CP was performed early.[10] This remarkable high rate of post CP hydrocephalus in the late CP group is not reported in the other included studies of the meta-analysis, explaining the high heterogeneity in the meta-analysis of all pathologic subgroups together (I^2 = 62%).[1-4,6,8,11-13,16] To address such high heterogeneity, Cochrane proposed to exclude the most outlying study, after performing a random effects meta-analysis.[4] If doing so and excluding the cohort study from Nasi *et al*., early CP for all pathologic conditions together is associated with a higher incidence of post CP hydrocephalus.[5] (OR 2.49; 95% CI 1.59–3.91; I^2 = 0%) [Figure 2].[1-4,6,8,11-13,16]

How to define post CP hydrocephalus?

The goal of the meta-analysis by Nasi and Dobran was to investigate the influence of timing of CP after decompressive craniectomy on post CP hydrocephalus. A fundamental issue, while reviewing studies reporting on the incidence of hydrocephalus following early and late CP, is the exact definition of post CP hydrocephalus. If a patient with pre CP hydrocephalus undergoes CP and subsequently requires implantation of a permanent CSF shunt, does one classify this as post CP hydrocephalus? In our recently published study on 145 patients undergoing CP, 26 suffered from pre CP hydrocephalus and received external CSF drainage. After CP, 13 of these patients required post CP ventriculoperitoneal (VP) shunt implantation (10/37 early CP patients and 3/108 late CP patients). Since these shunt placements were more or less "foreseen," we did not classify them as post CP hydrocephalus. Instead, only post CP VP shunt implantations in patients without symptomatic disturbance in CSF flow prior to CP were classified as post CP hydrocephalus, which occurred in one patient of the early CP group.[4] This latter number was thus included in the current meta-analysis by Nasi and Dobran.[9] However, one could argue that the previous 13 patients receiving foreseen post CP VP shunt implantation for hydrocephalus are also to be classified as post CP hydrocephalus. Such definition would considerably influence the outcome results of the meta-analysis of the

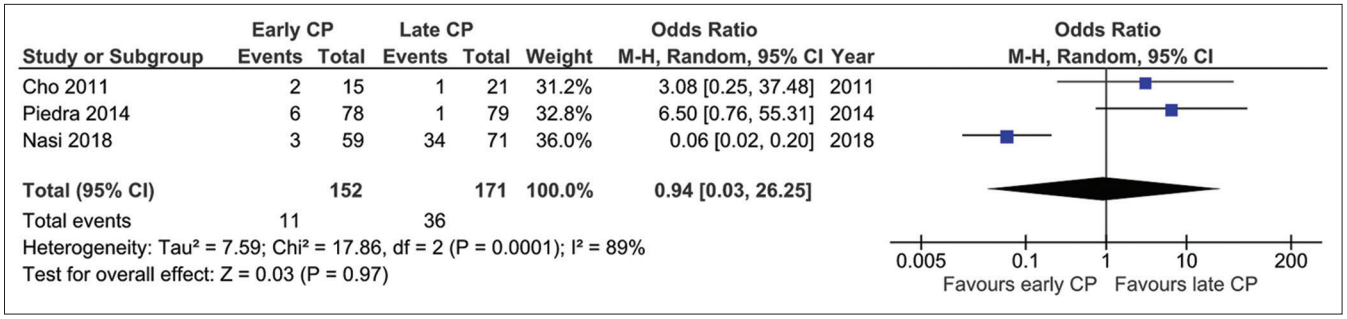

Figure 1: Random effects meta-analysis of hydrocephalus rate in patients undergoing early (within 3 months) versus late (after 3 months) cranioplasty after decompressive craniectomy for traumatic brain injury.

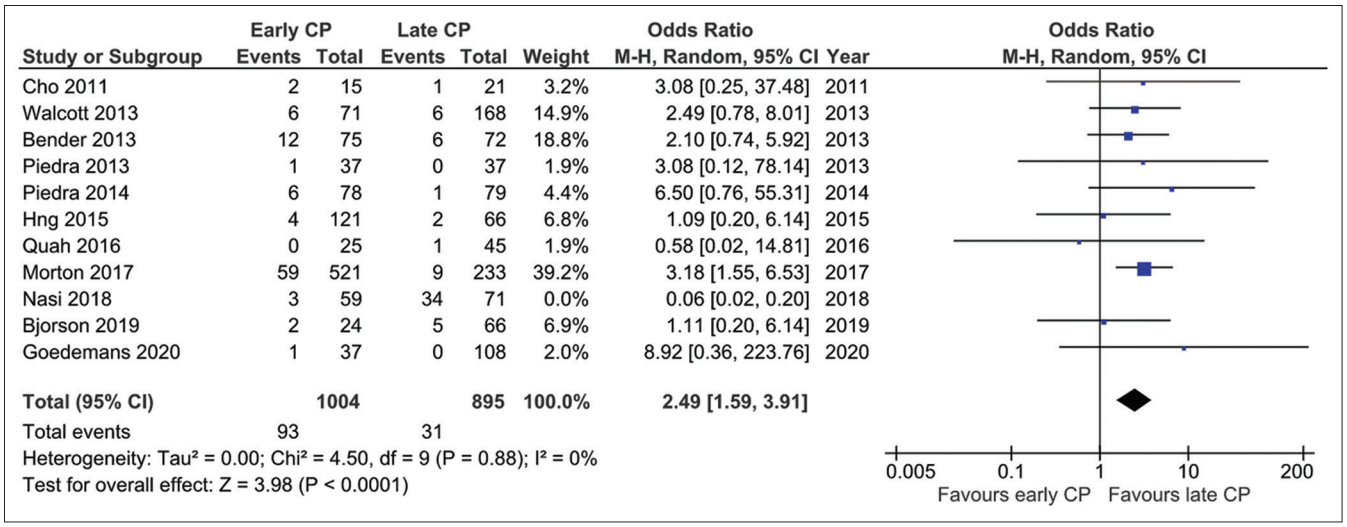

Figure 2: Meta-analysis of hydrocephalus rate in patients undergoing early (within 3 months) versus late (after 3 months) cranioplasty after decompressive craniectomy for all pathologic conditions, with exclusion of outlying outcome result by Nasi *et al*.[10]

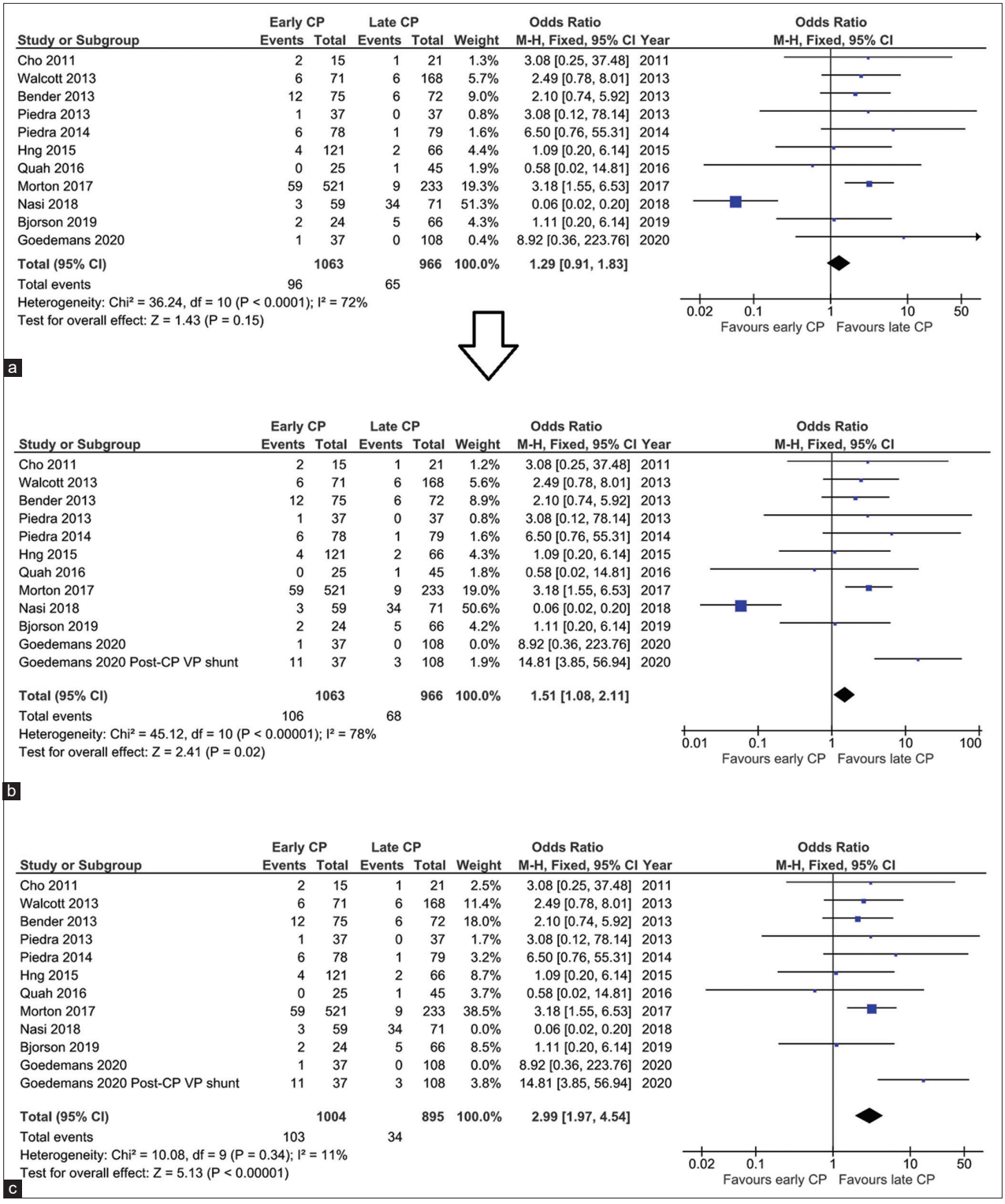

Figure 3: Meta-analysis of hydrocephalus rate in patients undergoing early (within 3 months) versus late (after 3 months) cranioplasty (CP) after decompressive craniectomy for all pathologic conditions; (a) hydrocephalus rate reported as new seen after CP by Goedemans *et al.*[4]; (b) hydrocephalus rate reported as the need for post CP ventriculoperitoneal (VP) shunt placement, derived from Goedemans *et al.* (i.e., including "foreseen" VP shunt placements due to pre CP hydrocephalus)[4]; (c) hydrocephalus rate reported as the need for post CP VP shunt placement, derived from Goedemans *et al.* (i.e., including "foreseen" VP shunt placements due to pre CP hydrocephalus)[4], with exclusion of outlying outcome result by Nasi *et al.*[10]

influence of timing of CP for all pathologic conditions together, which is illustrated in [Figure 3] (The results then change from not significant [Figure 3a] to significant [Figure 3b] and the results remain significant when excluding the most outlying study from Nasi *et al*. [Figure 3c]). How did the other research groups define post CP hydrocephalus? Did they consider all post CP implanted permanent CSF shunts as post CP hydrocephalus? Or did they account for the confounder "presence of pre CP hydrocephalus?" Unfortunately, none of the other studies reported data on the presence of pre CP hydrocephalus.[1-4,6,8,11-13,16]

CONCLUSION

Based on the abovementioned comments, revision of the conclusions drawn by Nasi and Dobran seems warranted as random effects meta-analysis shows that early CP in TBI patients is *not* associated with a lower incidence of hydrocephalus. To analyse the true association between the timing of CP and hydrocephalus as a complication seen after CP, the rate of pre CP hydrocephalus must be taken into account.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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