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Original Articles

A Consensus-Based Interpretation of the Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure Trial

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Abstract

Widely-varying published and presented analyses of the Benchmark Evidence From South American Trials: Treatment of Intracranial Pressure (BEST TRIP) randomized controlled trial of intracranial pressure (ICP) monitoring have suggested denying trial generalizability, questioning the need for ICP monitoring in severe traumatic brain injury (sTBI), re-assessing current clinical approaches to monitored ICP, and initiating a general ICP-monitoring moratorium. In response to this dissonance, 23 clinically-active, international opinion leaders in acute-care sTBI management met to draft a consensus statement to interpret this study. A Delphi method–based approach employed iterative pre-meeting polling to codify the group's general opinions, followed by an in-person meeting wherein individual statements were refined. Statements required an agreement threshold of more than 70% by blinded voting for approval. Seven precisely-worded statements resulted, with agreement levels of 83% to 100%. These statements, which should be read in toto to properly reflect the group's consensus positions, conclude that the BEST TRIP trial: 1) studied protocols, not ICP-monitoring per se; 2) applies only to those protocols and specific study groups and should not be generalized to other treatment approaches or patient groups; 3) strongly calls for further research on ICP interpretation and use; 4) should be applied cautiously to regions with much different treatment milieu; 5) did not investigate the utility of treating monitored ICP in the specific patient group with established intracranial hypertension; 6) should not change the practice of those currently monitoring ICP; and 7) provided a protocol, used in non-monitored study patients, that should be considered when treating without ICP monitoring. Consideration of these statements can clarify study interpretation.

Key words: BEST TRIP trial; Consensus Development Conference; intracranial pressure; neurocritical care; traumatic brain injury

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PUBLICATION of the Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (BEST TRIP) trial[1] has resulted in significant controversy in the treatment of severe traumatic brain injury (sTBI). This randomized controlled trial of intracranial pressure (ICP)–based management versus management guided by serial computed tomography (CT) imaging and clinical examination without ICP monitoring tested the primary hypothesis that ''a management protocol based on the use of intracranial-pressure monitoring would result in reduced mortality and improved neuropsychological and functional recovery at 6 months.'' It reported no significant between-group difference in morbidity or mortality measured at six months post-injury. Publicly-presented interpretations of the clinical implications of this study have ranged from statements that the BEST TRIP trial is irrelevant to treatment in high-income countries due to its being conducted in Latin American low-income countries, through questioning of the indications for ICP measurement, to calls for a moratorium on ICP monitoring. Public health implications have included limitation of insurance reimbursement for ICP monitors in Brazil. Interpretation also has varied widely in published analyses.[2–18]

There is a paucity of studies amenable to resolving such controversy in this area, as summarized in the Guidelines for the Management of Severe Traumatic Brain Injury in Adults from the Brain Trauma Foundation (BTF).[19] Accordingly, a group consensus statement would be valuable in addressing the interpretation of this study, the only large-scale, high-quality randomized controlled trial on the topic. To develop such consensus, a Delphi method–based meeting occurred in Seattle Washington, on September 6–8, 2013. A committee (the authors' group) was selected from international opinion leaders who are currently active in both bedside patient management and clinical research. Two professional meeting facilitators were employed to ensure that the pre- and intra-meeting methods addressed all topics originated by the participants during discussion, recorded and represented all whole- and small-group discussions in the consensus process, reflected input from all participants, and that the final statements accurately reflect unbiased group writing, editing, and consensus ratification processes. Before the meeting, three surveys were conducted to poll the overall opinions of the group regarding the interpretation and implications of the study. The collected responses were consolidated into two ''straw man'' summations—''What the BEST TRIP trial showed'' and ''Interpretation of the BEST TRIP trial''—which were used to initiate whole-group and small-group discussions. Summaries from these iterations were condensed into working summary statements, which the group then discussed, refined and subjected to iterative blinded voting, targeting a consensus agreement of more than 70%. All issues felt relevant were developed into statements, which were iterated to consensus. No minority or dissenting opinions arose to produce statements that were rejected due to lack of consensus. Although the statement-generating nature of this process may have been insensitive to such dissention, the consensus figures reached for the final statements support strong group agreement. This process produced the following set of consensus statements:

Statement 1 (100% Consensus)

The BEST-TRIP trial compared two management protocols for treatment of severe TBI: one involving ICP monitoring and the other involving serial CT imaging and neurologic examination. It was not a trial of ICP monitoring or the efficacy of ICP monitoring.

Statement 2 (100% Consensus)

For the collective group of severe TBI patients meeting BTF criteria for ICP monitoring, the BEST TRIP trial found no difference in outcome between patients treated following ICP monitoring and treatment according to current BTF guidelines and patients treated according to a novel standardized protocol of sequential CT imaging and clinical examination modeled on local standard of care. As a consequence, this trial should be regarded as a study of two methods of severe traumatic brain injury management. Questions regarding sample size remain a concern, particularly with reference to the ability of this study to determine equivalence or rule out treatment effects that are more subtle or specific to selected patient subgroups.

Statement 3 (100% Consensus)

The primary impact of the BEST TRIP trial should be research oriented, suggesting that further investigation is necessary in the areas of selection of patients for ICP monitoring, determination of patient-specific ICP thresholds, and development of treatment methods and paradigms.

Statement 4 (94% Consensus)

The BEST TRIP trial is a study with high internal validity. The external validity of the BEST TRIP trial is low, primarily due to concerns regarding generalizability arising from unquantified uncertainties surrounding the influence of the prehospital environment on the composition of the study group. Additional questions arise from treatment options in the ICP group.

Statement 5 (94% Consensus)

ICP monitoring was tested in a broad group of patients with severe TBI who did not all have intracranial hypertension. Thus, the role of ICP monitoring in directing the treatment of established intracranial hypertension was not a focus of the BEST TRIP trial.

Statement 6 (94% Consensus)

For those currently monitoring ICP, the results of the BEST TRIP trial should not change their practice.

Statement 7 (83% Consensus)

This multicenter randomized trial also showed that the use of the previously unstudied Imaging and Clinical Examination (ICE) protocol in a hospital with limited economic resources that preclude the availability of intracranial pressure monitoring may lead to non-inferior clinical outcomes, compared with the BTF guidelines-driven control of ICP using intracranial pressure monitoring.

The committee agreed that these statements represent the aggregate opinion of the group.

It must be stressed that these statements reflect a consensus core acceptable to all participants but not necessarily reflecting the opinion of any individual author. Many differing opinions can be woven around this core. Its main purpose is to orient the analytic process upon the data as presented in the publication. It is expressly not intended to inhibit varying analyses or define the range of interpretations.

We hope that these statements will serve as a reference to practicing physicians, researchers, and clinical associations in guiding the interpretation of the BEST TRIP results and mitigating what one committee member termed ''collateral damage'' from its

misunderstanding. Further consensus recommendations are presently in preparation regarding clinical and research approaches to ICP monitoring and treatment in light of current data.

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