A Systematic Review and Meta-analysis of Intra Aortic Balloon Pump Therapy in ST-elevation Myocardial Infarction. Should we change the Guidelines?

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ABSTRACT

The body of evidence supporting IABP therapy in STEMI and in STEMI with cardiogenic shock remains limited. We conducted two meta-analyses respectively comparing IABP therapy with no IABP therapy for the treatment of STEMI and the treatment of STEMI complicated by cardiogenic shock. The principal findings of the meta-analysis of randomized clinical trials of IABP therapy in STEMI showed no efficacy benefit of adjunctive IABP therapy. We neither observed a 30-day survival benefit nor improved left ventricular ejection fraction. Instead, IABP therapy was associated with a significant absolute increase in the rates of stroke and bleeding of respectively 2% and 6%. These clinically relevant higher complication rates are not outweighed by any clinical benefit.

META-ANALYSIS

In the absence of randomized studies, we performed a separate meta-analysis of all available observational studies comparing IABP therapy versus no IABP therapy in STEMI complicated by cardiogenic shock. The most striking observation in this meta-analysis was the heterogeneity in the effect estimates of IABP therapy between the thrombolysis and the primary PCI studies. The overall effect estimate in the thrombolysis cohorts favoured IABP therapy, whereas the overall effect estimate in the primary PCI cohorts disfavoured IABP therapy. This observation does not render support to the concept that potential beneficial effects of IABP on outcome in STEMI complicated by cardiogenic shock would be independent of the type of reperfusion therapy.

The observed beneficial effect of IABP therapy as an adjunct to thrombolysis would support the rationale for IABP therapy of myocardial and organ recovery. Furthermore, it would support the hypothesis that IABP increases the efficacy of thrombolytic therapy in STEMI patients with cardiogenic shock by increasing coronary perfusion. However, there are at least three other explanations for the observed lower mortality in the IABP group in this setting. First, the IABP treated patients were on average seven years younger and the frequency of men was 10% higher. As known from current literature the odds for mortality increase by 49 to 60% for every 10 years increase in age. Second, in the thrombolysis studies co-treatment with coronary revascularization was substantially more frequent in patients who received IABP therapy than in patients who did not receive IABP therapy. The SHOCK trial clearly showed that revascularization effectively reduced mortality in cardiogenic shock patients. The revascularization rates in the SHOCK trial in the emergent revascularization arm and the conservative medical treatment arm respectively were 87% and 25% (relative risk 3.4), whereas the rate of IABP therapy was 86% in both groups. In comparison, the overall revascularization rates in the thrombolysis studies from the meta-analysis in the IABP and no IABP group were 39% and 9% (relative risk 4.0), respectively. Third, in the thrombolysis studies, the sicker patients may have been considered too ill to benefit from IABP therapy and others may have died before they could receive IABP therapy. In summary, the lower mortality of the patients who received IABP adjunctive to thrombolysis, can be explained by confounding and bias, rather than by a beneficial effect of IABP therapy per se.

DETRIMENTAL EFFECT

The observed detrimental effect of IABP therapy as an adjunct to primary PCI in STEMI with cardiogenic shock is contrary to the expectation that IABP might improve survival in these patients. It would oppose the suggestion that underutilization of IABP therapy is one of the causes of the remainingly high mortality in this setting. However, there are two important issues that need to be addressed concerning the outcome of IABP therapy in the primary PCI cohorts. First, we cannot rule out the influence of confounders in non-randomized studies. Nevertheless, in the NRMI-2 cardiogenic shock cohort, IABP therapy was independently associated with a higher 30-day mortality after multivariate adjustment for age, several clinical risk factors, PCI and CABG. Second, IABP therapy may have been preferentially given to patients in worse condition. In a catheterization setting it is difficult to withhold patients from active treatment with IABP, even if their prognosis is extremely grim.

Alternatively, the negative treatment effect of IABP therapy could also reflect a longer ischemic time, as IABP support may have been used for transfer to a primary PCI facility. Either way, these phenomena may have induced a severe bias towards poor outcomes in the IABP group, which is in contrast to the bias noted in the thrombolysis studies. In summary, one cannot reliably distinguish between an unexpected, truly detrimental effect of IABP therapy as an adjunct to primary PCI in STEMI complicated by cardiogenic shock and the influence of bias and confounding inherent to cohort studies. Therefore the results of this analysis must be interpreted cautiously.

FINDINGS

Our findings may have several implications for the clinical practice guidelines and ongoing research. Currently the ACC/AHA and ESC guidelines do not explicitly address the use of IABP therapy in high risk STEMI. The pooled randomized data do not support IABP therapy in this setting. As many practitioners still use IABP therapy in high risk STEMI patients, a guideline statement about IABP therapy according to the appropriate classification of recommendation and level of evidence should be considered for this indication.

CARDIOGENIC SHOCK

Cardiogenic shock, when not quickly reversed by pharmacologic therapy, is listed in the ACC/AHA guidelines as a class IB recommendation. The ESC guidelines also strongly recommend IABP therapy in STEMI with cardiogenic shock. Our study challenges these recommendations. Combining both meta-analyses, one may conclude that there is insufficient evidence endorsing the current recommendation for IABP therapy in STEMI with cardiogenic shock. Hence, any recommendation for adjunctive IABP therapy at this time can be based on expert opinion only. Concomitant IABP therapy along with other various available pharmacologic and mechanical therapeutic means may have some specific indications in cardiogenic shock patients. However, this study implies that greater nuances with regard to IABP therapy in this setting are needed than given in the current guidelines.

TREATMENT OF STEMI

Ultimately, to clarify its role in contemporary treatment of STEMI with cardiogenic shock, including stenting and the use of glycoprotein IIb/IIIa inhibitors, a randomized controlled trial of IABP therapy versus no support adjunctive to primary percutaneous coronary intervention should be undertaken. After all, mechanical cardiac assist, due to its intuitive and experimentally supported rationale, remains an appealing treatment strategy. Especially since mortality in cardiogenic shock is still unacceptably high. The recent introduction of percutaneous left ventricular assist devices is very promising. They may be a superior alterna-

tive to IABP therapy. However, as we can learn from the TRIUMPH trial and two recent trials on mechanical cardiac assist, we should realize that improved hemodynamic status, either pharmacologically or mechanically induced, is not a surrogate marker for survival. Therefore, also for these new devices we need evidence from properly powered randomized controlled trials with regard to their effect on outcome, before we herald these devices as a new therapeutic option.

CONCLUSION

The meta-analysis of randomized studies did not support the use of routine IABP in high risk STEMI. The meta-analysis of cohort studies in the setting of STEMI complicated by cardiogenic shock supported IABP therapy adjunctive to thrombolysis. In contrast, the observational data did not support IABP therapy adjunctive to primary PCI. All available observational data concerning IABP therapy in the setting of cardiogenic shock is importantly hampered by bias and confounding. There is insufficient evidence endorsing the current guideline recommendation for the use of IABP therapy in the setting of STEMI complicated by cardiogenic shock. Our meta-analyses challenge the current guideline recommendations.