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Intra-aortic Balloon Pump: Reviewing its Role in Cardiogenic Shock

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Abstract: Cardiogenic shock is a high-mortality condition caused, mostly, by ST-elevation myocardial infarction. When the adequate therapy is implemented in a timely fashion, recovery can be achieved. Treatment is based on intensive care measures, vasoactive drugs, early revascularization and the use of assist circulatory devices. In this review, the authors aim to discuss the available evidence on the use of intra-aortic balloon pump (IABP) in this clinical setting.

Keywords: Intra-aortic balloon pump, Counterpulsation, Myocardial infarction, Cardiogenic shock, Mortality, Complications.

INTRODUCTION

Cardiogenic shock (CS) is a condition with a high mortality rate - around 50% [1] -, defined by a state of tissue malperfusion caused by heart failure (HF) and complicates up to 8% of cases of ST-elevation myocardial infarction (STEMI) [2,3]. Although a critical condition, it can be reversed if the proper set of therapies is instituted in time and the correct identification of in-risk patients is made. Therefore, some risk factors related to the development of CS in patients with an acute myocardial infarction (AMI) must be emphasized: older age, anterior MI, hypertension, diabetes, multivessel coronary heart disease, prior MI or HF and left bundle-branch block [4].

Treatment of CS is based, mainly, on coronary reperfusion; more specifically, on early revascularization (percutaneous coronary intervention – PCI – or coronary artery bypass graft – CABG). The survival benefit of non-delayed revascularization was clearly demonstrated in the randomized "Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock" (SHOCK) trial, with an absolute increase of 13% in 1-year survival compared to those assigned to initial clinical stabilization [5, 6].

However, mechanical circulatory support is, in a large proportion of cases, an important adjunctive therapy. In such cases, the most commonly used device is the intra-aortic balloon pump (IABP). There are evidence both demonstrating its benefits as well as showing no advantage in the setting of CS. [7-17].

INTRA-AORTIC BALLOON PUMP

Intra-aortic balloon pump is the most commonly used mechanical support device to improve circulatory hemodynamics in cardiogenic shock. Based on the principle of counterpulsation, it was first clinically applied in the late 1960s, by Kantrowitz *et al*. [18]. In the early 1980s [19] its use became widespread since the development of a percutaneous approach for insertion

It is composed of a flexible catheter with a lumen that permits pressure monitoring, and a second one that allows the periodic in- and outflow of helium gas to a polyethylene balloon; also a console which contains the helium transfer system and an electronic control for the inflation-deflation cycle.

The catheter is inserted through the common femoral artery and advanced - either at the bedside or under fluoroscopic guidance in the cath lab - so the distal tip is positioned in the proximal descending aorta - 1-2 cm below the emergence of the left subclavian artery - and the proximal portion is placed above the renal arteries. The console controls the pumping using input from the aortic pressure and/or the electrocardiogram. Inflation occurs just after aortic

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valve closure, and deflation must happen immediately before aortic valve opening

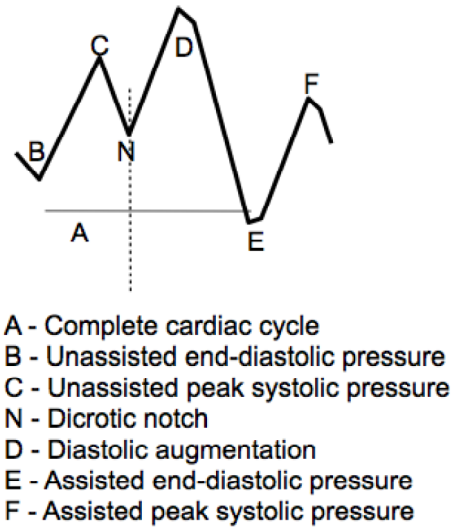

Figure 1: Cardiac cycle and normal timing of IABP inflation - dotted line).

The hemodynamic effects depend on the appropriate balloon size and timing of the inflation-deflation cycle. When properly set, the use of IABP results in: decrease in systolic pressure (during balloon deflation, consequence of a reduction of left ventricle after load); increase in diastolic pressure (during balloon inflation, which raises coronary blood flow); reduction of heart rate (in nearly 10-20%); and elevation of cardiac output [20]. The net result is an improvement in cardiac energy balance, with a decrement in myocardial oxygen demand and augmentation of oxygen supply [21].

According to the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of STEMI, the use of IABP can be useful for those with CS in this setting who do not quickly stabilize with pharmacological therapy [22], receiving a Class II a recommendation. Noteworthy is the fact that IABP use in CS was downgraded in relation to the earlier edition of those guidelines [23], where it used to receive a Class IB recommendation.

Data regarding complications associated with IABP are difficult to be summarized as a general topic because of the heterogeneity of studies - not only regarding study population, but also in the definitions of such complications. However, it is known that vascular complications - arterial laceration with need of surgical repair, limb ischemia (with eventual amputation) and major bleeding - are the most common IABP-related complications. Embolization, infection and IABP rupture may also occur. In the Benchmark Registry, the authors evaluated 22,663 consecutive patients in whom an IABP was inserted at 250 centers worldwide from 1996 to 2001, and Stone *et al*. [24] analyzed the 5,495 of those subjects who had an MI. In their study, one or more complications of IABP use occurred in 8.1% of patients, although major complications (severe limb ischemia - requiring surgical therapy -, severe bleeding - need of blood transfusion/surgical intervention or associated with hemodynamic compromise -, balloon leak or death directly due to IABP insertion or failure) occurred in only 2.7% of cases. Regarding those patients in whom IABP was used for CS, the rate of major complications was 2.9%. Ferguson *et al*. [25], in a previous publication of the same Registry, performed a multivariate logistic regression analysis to identify independent predictors of a major IABP-related complication. The results showed that female gender (OR 1.968; CI 1.557 - 2.487), peripheral vascular disease (OR 1.737; CI 1.414 - 2.134), small body surface area (BSA; <1.65 m^2) (OR 1.453; CI 1.095 - 1.926) and higher age (≧75 years) (OR 1.289; CI 1.048 - 1.585) were significantly related to an increased risk of such events.

INTRA-AORTIC BALLOON PUMP IN CARDIOGENIC SHOCK

Data regarding the use of IABP in patients with cardiogenic shock complicating an MI are controversial and the majority of positive results come from observational non-controlled studies. This was thought to be the reason for the low (<40%) use of IABP in this clinical scenario [26].

O`Rourke *et al*. [7], in 1981, studied the value of IABP in patients with early MI complicated by acute heart failure. Thirty patients were randomized to IABP or standard therapy, and no significant difference between groups was seen in infarct size, morbidity or mortality during a mean follow-up of 15 months.

In the analysis of 200 consecutive patients at Duke University with MI-related CS, between 1987 and 1988, 99 subjects used IABP [8]; the in-hospital mortality was lower (48% x 57%; p=0.23) in those who used IABP than in those who did not. Stomel *et al.* [9] examined 64 consecutive patients with MI and CS dividing the patients in three groups: thrombolytic therapy, IABP and combined thrombolysis plus IABP. The groups were similar in regard to age, sex, medical history,

hemodynamic data and extent of coronary artery disease. Survival was improved in patients treated with combined thrombolytic therapy and IABP support (23% x 28% x 68%, respectively; p=0.0049).

More than 40,000 subjects were enrolled in the "Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries" (GUSTO I) trial, and all were eligible for thrombolytic therapy. A small percentage (7%; n=2,972) developed CS after STEMI [10]. Therapy included the use of IABP in 734 patients. The results showed that early insertion of IABP in these patients was related to a non-significant decrease in mortality compared to those cases in which it was used with delay or not inserted (47% x 60%; p=0.06). In the same year, Hochman *et al*. reported data from the SHOCK Registry [11] analyzing 251 patients from 19 American and Belgian centers where both thrombolysis and mechanical revascularization were used. Patients in whom IABP was used were significantly younger, more often underwent coronary angiography and had no benefit in adjusted mortality compared to those in whom IABP was not used (p=0.66). This lack of benefit in mortality also occurred in those who underwent coronary angioplasty (62% with IABP x 54% without IABP; p=0.743).

A later analysis of 856 subjects from 36 participating centers in the SHOCK Trial Registry showed lower mortality rates in those who used IABP compared to those who did not (50% x 72%; p< 0.0001), and in the group treated with the combination of thrombolytic plus IABP compared to the one who did not receive nor thrombolytic nor IABP (47% x 77%; p< 0.0001) [12]. Similarly, in a retrospective analysis of data from the SHOCK trial, French *et al*. [13] observed a reduction in 1-year mortality, yet not statistically significant, in those patients assigned to initial medical stabilization who received the combination of thrombolysis and IABP compared to those who did not use IABP (41% x 64%; p=0.07).

One crucial aspect when performing invasive procedures is the level of expertise presented by hospitals and their staff. This point was addressed by Chen *et al*. [14] using data from over 12,000 patients enrolled in the National Registry of Myocardial Infarction (NRMI) in the mid 1990`s. In their paper, the authors demonstrated that patients treated in hospitals with a high IABP volume had lower mortality (OR 0.71; 95% CI 0.56-0.90) regardless of other factors.

In the TACTICS trial [15], 57 subjects were randomized to fibrinolytic therapy alone or the combination of fibrinolysis plus IABP. The primary endpoint was all-cause mortality in 6 months and the results showed no significant difference between groups (34% for combination x 43% for fibrinolysis alone; p=0.23) but a trend toward significant benefit in this same outcome when combination therapy was used in those with more severe conditions (Killip III/IV) - 39% x 80% 6-month mortality, respectively; p=0.05). In 2009, Sjauw *et al*. [16] performed two different analyses with previous studies in patients with CS following STEMI: the first one was restricted to data from randomized trials, in a total of seven trials and 1,009 patients; the other included nine cohorts with more than 10,000 subjects. The results from the first analysis showed no advantage of IABP in 1-month survival - but higher rates of stroke and bleeding. In the second analysis, the use of IABP in patients treated with thrombolysis was related to an 18% lower mortality in 30 days (95% CI 16-20; p<0.0001); however, in those treated with primary PCI, IABP was associated with a 6% increase in the same endpoint (95% 3-10; p<0.0008). The authors concluded the article challenging the available guideline recommendations at that time.

More recently, the IABP-SHOCK II trial was published with the aim to answer the question if IABP was capable of reduce mortality in patients with CS following MI for whom early revascularization was planned [17]. It was a multicenter, open-label, randomized study where 600 patients were randomly assigned (1:1 ratio) to IABP or non-IABP and were expected to be treated with early revascularization (primary PCI with treatment of the target lesion only, PCI of the target lesion plus additional immediate or staged PCI of nontarget lesions, or CABG at the discretion of the operator). There was no difference in the primary outcome (30-day mortality) among groups (39.7% IABP x 41.3% non-IABP; RR with IABP 0.96, 95% CI 0.79-1.17; p=0.69). In terms of safety, there was no significant difference between groups with respect to the rates of stroke, bleeding, sepsis or vascular complications requiring intervention.

CONCLUSIONS

When faced with such condition, one must keep in mind the considerable severity inherent to it, where pump failure is the primary derangement but other parts of the circulatory system play a role with inadequate compensation or additional defects [27]. Another point to be remembered is that the cornerstone in the treatment of such cases is early

revascularization; the use of assist circulatory devices is an adjunctive therapy - and nothing more.

Compared to other devices, *e.g*. TandemHeart and Impella, IABP does not need a surgeon to be inserted. It can be inserted either under fluoroscopic guidance or at the bedside by the interventional cardiologist, clinical cardiologist or intensive care physician. Studies in which patients were randomly assigned to treatment with IABP or TandemHeart showed that latter was related to an increase risk – significantly [28] and non-significantly [29] – of severe bleeding. When it comes to the comparison between Impella and IABP, Seyfath *et al*. [30] found similar results. Noteworthy is the fact that both TandemHeart and Impella had better hemodynamic data than IABP, although this was not translated into significantly lower mortality.

Considering the high costs involved in the treatment of patients with myocardial infarction complicated by cardiogenic shock, and the net results demonstrated so far by newer, more expensive devices, IABP might still be the most cost-effective option in this clinical setting.

Although the recent downgrade in the recommendation for its use in this setting, IABP may be the assist circulatory device with the best combination of ease of insertion and handling, lower complication rates, potential benefits in terms of hemodynamics and outcomes and cost-effectiveness.

REFERENCES

[1] Goldberg RJ, Gore JM, Thompson CA, Gurwitz JH. Recent magnitude of and temporal trends (1994–1997) in the incidence and hospital death rates of cardiogenic shock complicating acute myocardial infarction: the second national registry of myocardial infarction. Am Heart J 2001; 141: 65–72. http://dx.doi.org/10.1067/mhj.2001.111405

[2] Fox KA, Anderson FA Jr, Dabbous OH, Steg PG, Lopez-Sendon J, Van de Werf F, Budaj A, Gurfinkel EP, Goodman SG, Brieger D. Intervention in acute coronary syndromes: do patients undergo intervention on the basis of their risk characteristics? The Global Registry of Acute Coronary Events (GRACE). Heart. 2007; 93: 177-182. http://dx.doi.org/10.1136/hrt.2005.084830

[3] Babaev A, Frederick PD, Pasta DJ, Every N, Sichrovsky T, Hochman JS. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. JAMA. 2005; 294: 448-454. http://dx.doi.org/10.1001/jama.294.4.448

[4] Lindholm MG, Kober L, Boesgaard S, Torp-Pedersen C, Aldershvile J. Cardiogenic shock complicating acute myocardial infarction: prognostic impact of early and late shock development. Eur Heart J. 2003; 24: 258-265. http://dx.doi.org/10.1016/S0195-668X(02)00429-3

[5] Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, McKinlay SM, LeJemtel TH. Early revascularization in acute myocardial infarction complicated by cardiogenic shock: SHOCK Investigators: Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. N Engl J Med. 1999; 341: 625– 634. http://dx.doi.org/10.1056/NEJM199908263410901

[6] Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, Col J, White HD. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. JAMA. 2006; 295: 2511-2515. http://dx.doi.org/10.1001/jama.295.21.2511

[7] O'Rourke MF, Norris RM, Campbell TJ, Chang VP, Sammel NL. Randomized controlled trial of intraaortic balloon counter-pulsation in early myocardial infarction with acute heart failure. Am J Cardiol 1981; 47: 815-820. http://dx.doi.org/10.1016/0002-9149(81)90179-X

[8] Bengtson JR, Kaplan AJ, Pieper KS, Wildermann NM, Mark DB, Pryor DB, Phillips HR, 3rd, Califf RM. Prognosis in cardiogenic shock after acute myocardial infarction in the interventional era. J Am Coll Cardiol 1992; 20: 1482-1489. http://dx.doi.org/10.1016/0735-1097(92)90440-X

[9] Stomel RJ, Rasak M, Bates ER. Treatment strategies for acute myocardial infarction complicated by cardiogenic shock in a community hospital. Chest 1994; 105: 997–1002. http://dx.doi.org/10.1378/chest.105.4.997

[10] Holmes DR, Jr, Bates ER, Kleiman NS, Sadowski Z, Horgan JH, Morris DC, Califf RM, Berger PB, Topol EJ for the GUSTO-I Investigators. Contemporary reperfusion therapy for cardiogenic shock: the GUSTO-I trial experience. Global Utilization of Strep- tokinase and Tissue Plasminogen Activator for Occluded Coro- nary Arteries. J Am Coll Cardiol 1995; 26: 668-674. http://dx.doi.org/10.1016/0735-1097(95)00215-P

[11] Hochman JS, Boland J, Sleeper LA, Porway M, Brinker J, Col J, Jacobs A, Slater J, Miller D, Wasserman H, *et al*. for SHOCK Registry Investigators. Current spectrum of cardiogenic shock and effect of early revascularization on mortality. Results of an International Registry. Circulation 1995; 91: 873-881. http://dx.doi.org/10.1161/01.CIR.91.3.873

[12] Sanborn TA, Sleeper LA, Bates ER, Jacobs AK, Boland J, French JK, Dens J, Dzavik V, Palmeri ST, Webb JG, *et al*. Impact of thrombolysis, intra-aortic balloon pump counterpulsation, and their combination in cardiogenic shock complicating acute myocardial infarction: a report from the SHOCK Trial Registry. Should we emergently revascularize occluded coronaries for cardiogenic shock? J Am Coll Cardiol 2000; 36(3 Suppl A):1123-1129. http://dx.doi.org/10.1016/S0735-1097(00)00875-5

[13] French JK, Feldman HA, Assmann SF, Sanborn T, Palmeri ST, Miller D, Boland J, Buller CE, Steingart R, Sleeper LA, *et al*. Influence of thrombolytic therapy, with or without intra-aortic balloon counterpulsation, on 12-month survival in the SHOCK trial. Am Heart J 2003; 146: 804–810. http://dx.doi.org/10.1016/S0002-8703(03)00392-2

[14] Chen EW, Canto JG, Parsons LS, Peterson ED, Littrell KA, Every NR, Gibson CM, Hochman JS, Ohman EM, Cheeks M, *et al*. Relation between hospital intra-aortic balloon counterpulsation volume and mortality in acute myocardial infarction com- plicated by cardiogenic shock. Circulation 2003; 108: 951-957. http://dx.doi.org/10.1161/01.CIR.0000085068.59734.E4

[15] Ohman EM, Nanas J, Stomel RJ, Leesar MA, Nielsen DW, O`Dea D, *et al*. Thrombolysis and counterpulsation to improve survival in myocardial infarction complicated by hypotension and suspected cardiogenic shock or heart failure: results of the TACTICS Trial. J Thromb Thrombolysis. 2005; 19: 33-39. http://dx.doi.org/10.1007/s11239-005-0938-0

[16] Sjauw KD, Engström AE, Vis MM, *et al*. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-

elevation myocardial infarction: should we change the guidelines? Eur Heart J. 2009; 30: 459 - 68. http://dx.doi.org/10.1093/eurheartj/ehn602

[17] Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Böhm M, Ebelt H, Schneider S, Schuler G, Werdan K; IABP-SHOCK II Trial Investigators. N Engl J Med 2012; 367:1287-1296. http://dx.doi.org/10.1056/NEJMoa1208410

[18] Kantrowitz A, Tionneland S, Freed PS, *et al*. Initial clinical experience with intra-aortic balloon pumping in cardiogenic shock. JAMA 1968; 203: 135-140. http://dx.doi.org/10.1001/jama.1968.03140020041011

[19] Bregman D. A new percutaneous intra-aortic balloon. Trans Am Soc Artif Intern Organs 1980; 26: 8-11.

[20] Santa-Cruz RA, Cohen MG, Ohman EM. Aortic counterpulsation: a review of the hemodynamic effects and indications for use. Catheter Cardiovasc Interv 2006; 67:68-77. http://dx.doi.org/10.1002/ccd.20552

[21] Papaioannou TG, Stefanaids C. Basic principles of the intra-aortic balloon pump and mechanisms affecting its performance. ASAIO J 2005; 51: 296-300. http://dx.doi.org/10.1097/01.MAT.0000159381.97773.9B

[22] O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61: e78-140 http://dx.doi.org/10.1016/j.jacc.2012.11.019

[23] Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK. ACC/ AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). Circulation 2004; 110: e82–e292. 29 - Burkhoff D, Cohen H, Brunckhorst C, *et al*. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device ver- sus conventional therapy with intra-aortic balloon pumping for treatment of cardiogenic shock. Am Heart J 2006; 152: 469 e1– 469 e8. 30 - Seyfarth M, Sibbing D, Bauer I, Frõhlich G, Bott-Flˇugle L, Byrne R, *et al*. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for the treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol 2008 Nov 4; 52(19): 1584-1588. http://dx.doi.org/10.1016/j.jacc.2008.05.065

[24] Stone GW, Ohman EM, Miller MF, Joseph DL, Christenson JT, Cohen M, Urban PM, Reddy RC, Freedman RJ, Staman KL, *et al*. Contemporary utilization and outcomes of intra-aortic bal- loon counterpulsation in acute myocardial infarction: the bench- mark registry. J Am Coll Cardiol 2003; 41: 1940-1945. http://dx.doi.org/10.1016/S0735-1097(03)00400-5

[25] Ferguson JJ, Cohen M, Freedman RJ, *et al*. The current practice of intra-aortic balloon counterpulsation: results form the Benchmark Registry. J Am Coll Cardiol 2001; 38: 1456-62. http://dx.doi.org/10.1016/S0735-1097(01)01553-4

[26] Goldberg RJ, Samad NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM. Temporal trends in cardiogenic shock complicating acute myocardial infarction. N Engl J Med 1999; 340: 1162-1168. http://dx.doi.org/10.1056/NEJM199904153401504

[27] Reynolds HR, Hochman JS. Cardiogenic shock. Current concepts and improving outcomes. Circulation. 2008; 117: 686-97. http://dx.doi.org/10.1161/CIRCULATIONAHA.106.613596

[28] Thiele H, Sick P, Boudriot E, *et al*. Randomized compari- son of intra-aortic balloon support versus a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J 2005; 26: 1276-1283. http://dx.doi.org/10.1093/eurheartj/ehi16

[29] Burkhoff D, Cohen H, Brunckhorst C, *et al*. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device ver- sus conventional therapy with intra-aortic balloon pumping for treatment of cardiogenic shock. Am Heart J 2006; 152: 469 e1- 469 e8.

[30] Seyfarth M, Sibbing D, Bauer I, Frõhlich G, Bott-Flˇugle L, Byrne R, *et al*. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for the treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol 2008 Nov 4; 52(19): 1584-1588.

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