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Editorial Comment

Primary Angioplasty for Acute Myocardial Infarction—The Emerging Prognostic Role of Renal Insufficiency

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The outcomes of primary percutaneous coronary intervention (PCI) in patients with ST-elevation myocardial infarction (STEMI) and renal insufficiency have not been well characterized. One of the main reasons is that such patients have been typically excluded from clinical trials evaluating the outcome of coronary mechanical reperfusion performed in the acute phase of myocardial infarction [1,2]. Thus, only limited data deriving from a small number of studies are available to guide our therapeutic approach. As a result, no optimal treatment strategy has been defined for this subgroup of patients who represent a vulnerable population at higher morbidity and mortality risk. Some insights into this critical issue have been derived from the Controlled Abcximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial in which the clinical outcome of primary PCI as a function of renal insufficiency was evaluated [3]. Renal insufficiency, defined as a creatinine clearance (CrCl) $\leq$60 ml/min, was present in 350 patients (18%) who showed a >9-fold increase in mortality at 30 days, and a 5-fold increase in mortality at 1-year. The prognostic significance of serum creatinine concentration (sCr) in STEMI patients treated with primary PCI was also evaluated by a retrospective analysis of 1,451 patients drawn from the Heart Institute of Japan Acute Myocardial Infarction (HIJAMI) registry. According to this study, a graded increase of in-hospital death rate from 3.9% to 17.1% and 34.5% was found in patients with normal renal function (sCr <1.2 mg/dl), mild insufficiency (sCr >1.2 and $\leq$2.0 mg/dl), and severe insufficiency (sCr >2.0 mg/dl), respectively [4].

In this issue, Assali et al. [5] extend these observations, confirming the pervasive adverse influence of renal insufficiency in patients with STEMI undergoing primary PCI. The stepwise increase in 30-day mortality according to renal dysfunction severity observed in their population mirrors the previous results and further highlights the risk faced by these patients. The reduced survival of patients experiencing contrast-induced nephropathy, defined by the authors as a >25% increase in baseline sCr or as an absolute increase in sCr >0.5 mg/dl after primary PCI, represents another very important clinical message. In this setting, acute renal injury may be due to several factors. Impaired renal perfusion resulting from acute left ventricular dysfunction, intrinsic nephrotoxicity of contrast media particularly when a large volume of contrast is administered, dehydration and the impossibility of starting a renal prophylactic therapy may all play a pathogenetic role. The prognostic relevance of acute renal dysfunction in STEMI patients undergoing primary PCI was also observed in the CADILLAC trial [3]. Contrast-induced nephropathy developed in 4.6% of patients, being 3 times more frequent in patients with renal impairment, and was associated with a strikingly worse prognosis (30-day mortality of 16% and 1-year mortality of 23%). The incidence and clinical impact of contrast-induced nephropathy has been evaluated in our institute as well. Among 208 the STEMI patients treated with primary PCI, the rate of this complication was 19% (17% when patients with baseline increased sCr [>1.5 mg/dl] were excluded). However, of the 48 (23%) patients with baseline impaired renal function (CrCl <60 ml/min), 19 (40%) developed contrast-induced nephropathy and, conversely, of the 160 patients with a baseline CrCl value $\geq$60 ml/min, only 21 (13%) developed this complication. Thus, although the risk of contrast-induced nephropathy after primary PCI is significantly higher in patients with pre-existing renal failure, also those with normal baseline renal function may develop this complication. In our experience, patients with contrast-induced nephropathy had a more complicated in-hospital clinical course, and their average length of hospital stay was approximately 1.5 times longer than that of patients without it. The over-

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all in-hospital mortality in the entire population was 6.2%. However, the mortality rate was significantly higher in patients developing contrast-induced nephropathy than in those without it (31% vs. 0.6%).

The study by Assali et al. [5] should further increase our awareness of the prognostic role of renal insufficiency and the dire prognosis faced by STEMI patients with pre-existing kidney disease. However, it should not foster the attitude of "therapeutic nihilism" toward patients with renal failure who suffer STEMI nor suggest that thrombolysis may represent the best reperfusion modality [7,8]. It may be postulated that, if less aggressive therapy is provided, even worse outcomes may be expected and that pharmacological reperfusion therapies may be associated with increased incidence of major adverse events. Indeed, a pooled analysis of 16,710 patients receiving fibrinolytic therapy and enrolled in four studies (TIMI-10A, -10B, and -14, and inTIME-2) showed that patients with reduced renal function had both a stepwise decrease in survival, going from normal to mildly and severely impaired renal function, which continued up until 2 years of follow-up, and a higher rate of intracranial hemorrhage [9]. Thus, it is conceivable that, in patients with renal insufficiently, the potential benefit deriving from early reperfusion could be offset by a morbidity increase, particularly in terms of more bleeding complications after thrombolysis and a higher rate of contrast agent-induced nephropathy after primary PCI. All these data underscore the compelling need for innovative preventive approaches aimed at protecting the kidneys from contrast toxicity and ischemic burden when STEMI is treated with mortality-reducing therapies such as primary PCI. The recent demonstration that N-acetylcysteine may prevent contrast-induced nephropathy in STEMI patients undergoing primary PCI, and significantly improve their in-hospital outcome with a dose-dependent effect, is promising and adds some hope to the ongoing efforts to reduce the burden of risk in these patients and to ameliorate their poor outcome [10].

REFERENCES

1. Stone GW, Grines CL, Cox DA, et al. Comparison of angioplasty with stenting, with or without abcximab, in acute myocardial infarction. N Engl J Med 2002;346:957–966.
2. Grines CL, Cox DA, Stone GW. Coronary angioplasty with or without stent implantation for acute myocardial infarction.Stent Primary Angioplasty in Myocardial Infarction Study Group. New Engl J Med 1999;341:1949–1956.
3. Sadeghi HM, Stone GW, Grines CL, et al. Impact of renal insufficiency in patients undergoing primary angioplasty for acute myocardial infarction. Circulation 2003;108:2769–2775.
4. Yamaguchi J, Kasanuki H, Ishii Y, et al. Prognostic significance of serum creatinine concentration for in-hospital mortality in patients with acute myocardial infarction who underwent successful primary percutaneous coronary intervention (from the Heart Institute of Japan Acute Myocardial Infarction [HIJAMI] registry). Am J Cardiol 2004;93:1526–1528.
5. Assali AR, Brosh D, Ben-Dor I, et al. The impact of renal insufficiency on patients outcomes in emergent angioplasty for acute myocardial infarction. Catheter Cardiovasc Interv 2007;69:395–400.
6. Marenzi G, Lauri G, Assanelli E, et al. Contrast-induced nephropathy in patients undergoing primary angioplasty for acute myocardial infarction. J Am Coll Cardiol 2004;44:1780–1785.
7. Marenzi G, Assanelli E, Bartorelli AL. Management of acute coronary syndromes in patients with renal insufficiency. Curr Cardiol Rev 2006;2:11–16.
8. Dragu R, Behar S, Sandach A, et al. Should primary percutaneous coronary intervention be the preferred method of reperfusion therapy for patients with renal failure and ST-elevation acute myocardial infarction? Am J Cardiol 2006;97:1142–1145.
9. Gibson CM, Pinto DS, Murphy SA et al. Association of creatinine and creatinine clearance on presentation in acute myocardial infarction with subsequent mortality. J Am Coll Cardiol 2003;42:1535–1543.
10. Marenzi G, Assanelli E, Marana I, et al. *N*-acetylcysteine and contrast-induced nephropathy in primary angioplasty. N Engl J Med 2006;354:2773–2782.