demonstrated that plasma MCP-1 levels in 23 patients with acute myocardial infarction (MI) increase as early as 3 h after the onset of chest pain and reach their maximum at 24 h, with further gradual decline. We have no idea about the MCP-1 kinetics, because we did not examine the measurement of circulating MCP-1 in this study (1). Further studies will be needed on this important subject. In addition, in contrast to a previous experimental study (4)—which shows that Ly-6C^{lo} ($CD14^+CD16^+$ analogs) monocytes were found to be critical for myocardial healing via myofibroblasts accumulation, angiogenesis, and deposition of collagen—this study (1) did not show any significant effect of $CD14^+CD16^+$ monocytes on myocardial salvage followed by reperfused MI. However, we could not exclude the possibility that it might potentially be the result of a short period of observation (7 days after reperfusion).

We completely agree with Drs. Kavsak and and Jaffe's supposition that data in a more diverse group, including those with smaller events diagnosed with cardiac troponin, would be important to see whether difference exist between those groups. We also agree with their idea that data about monocyte subgroups would possibly determine the optical timing of intervention in patients with MI without ST-segment elevation (5). Well-designed prospective trials would highlight the effect of circulating distinct monocyte subsets on the optimal timing of intervention in patients for non–ST-segment elevation MI.

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Reply

We thank Drs. Kavsak and Jaffe for their discussion regarding the paper by Tsujioka et al. (1) and our accompanying editorial (2), and we agree that the role of monocytes in the pathogenesis of acute coronary syndromes (ACS) includes a lot of undiscovered areas. Although the significance of high monocyte count for the development of atherothrombotic events and unfavorable course of the recovery from them has been uniformly demonstrated, some controversy still exists in relation to the precise mechanisms responsible for monocyte recruitment to the damaged myocardium in general and monocyte chemoattractant protein (MCP)-1 in particular (3,4).

In addition to a small study by Matsumori et al. (5), other experimental and clinical studies support significant up-regulation of MCP-1 in ACS (as recently reviewed) (6). In the largest of such studies, the OPUS–TIMI (Orbofiban in Patients with Unstable coronary Syndromes–Thrombolysis In Myocardial Infarction) 16 trial (5), MCP-1 was significantly increased in 2,270 patients with ACS compared with stable subjects and was an independent prognostic factor for adverse outcomes (7).

Although the study by Kavsak et al. (8) on 216 patients with ACS did not reveal significant dynamics in MCP-1 at early stages of ACS, this work was limited by only 2 time-points included in the analysis (i.e., admission within 6 h after the onset of symptoms, and at 3 to 12 h later [median 6.5 h]), whereas monocytes are known to peak at 48 to 72 h after ACS onset. Additionally, the study did not include a stable control group and thus might not provide the basis to challenge the hypothesis that "prompt up-regulation of CCR-2 expressing CD14+CD16- monocytes" (2).

In fact, a critical role of MCP-1 for mobilization of monocytes from bone marrow and their homing to the sites of damage has been repeatedly shown. In contrast, mechanisms of recruitment of CD16+ monocyte population are less established. These cells can differentiate from CD16- monocytes or might be formed directly in bone marrow (9). Indeed, their biological role in human cardiac pathology is only scarcely analyzed. The many observations reported by Tsujioka et al. (1) (e.g., reduction of CD16+ monocytes in ACS patients at admission) do not have a robust explanation at present, thus raising further questions for future research. We agree with Drs. Kavsak and Jaffe that "data in a more diverse group" of ACS patients on the dynamics of monocyte subsets are needed to shed further light on their clinical implications.

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Imaging Surveillance for Cardiovascular Complications of Cancer Therapy

We read with great interest the state-of-the-art paper by Yeh and Bickford (1) on the cardiovascular complications of cancer therapy. Although the review on monitoring for chemotherapy associated left ventricular (LV) dysfunction discussed the role of established noninvasive tools, such as radionuclide ventriculography and echocardiography, evidence on emerging tools such as cardiac magnetic resonance (CMR) was not provided. The potential influence of cancer therapy on the vascular system was also not addressed.

CMR, with its heightened spatial resolution compared with these established modalities, has become a valuable tool in the assessment of myocardial function, perfusion, and tissue characterization (2). In addition, CMR has low intra- and interobserver variability and high test-retest reproducibility for measurement of LV function (3,4), characteristics that are crucial in clinical situations requiring accurate serial monitoring of LV function that occurs in cancer patients receiving potentially cardiotoxic therapy for cancer. Also, CMR is considered by the American College of Cardiology Foundation and multiple professional societies as an appropriate tool for evaluation of LV function in patients with technically suboptimal echocardiograms and evaluation of specific cardiotoxic therapy associated with cardiomyopathy (5).

Tissue characterization by CMR is a robust technique of prognostic importance (6). In a pilot study, Wassmuth et al. (7) demonstrated the strength of CMR to detect subclinical cardiotoxic effects of anthracyclines. Increase of relative myocardial contrast enhancement of >5 on day 3 compared with baseline predicted a significant decline in LV ejection fraction at 28 days ($p < 0.05$).

An emerging concern for cancer survivors is the increasing prevalence of cardiovascular events (8). For survivors of breast cancer and hematologic malignancies, cardiovascular events are the second most common cause of mortality after cancer recurrence (8). At present, there are few studies that have been performed to identify subclinical markers of increased cardiovascular events in cancer survivors. Increased aortic stiffness is an independent predictor of cardiovascular events beyond the Framingham score (9,10). In a soon-to-be published prospective case-control study, Chaosuwannakit et al. (11), observed a significant increase in CMR measures of aortic stiffness among cancer patients within 4 months of exposure to anthracycline chemotherapy. As cancer survivors experience higher incidence of cardiovascular events, further studies will be necessary to identify subclinical markers of cardiovascular disease.

CMR holds great potential in the comprehensive cardiovascular evaluation of cancer patients on therapy and should therefore be included in discussions on contemporary cardiovascular imaging of this growing patient population.

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