

THE AUTHORS REPLY: In our study of diverse radiologists in real-world practice, the use of CAD was not associated with an increase in cancer detection, which contrasts with prospective, single-facility studies in which experienced radiologists used CAD according to defined protocols.¹ We therefore concur with Gur that our study raises important questions about how community radiologists are trained to use CAD. For example, if some radiologists avert recalls on the basis of the absence of CAD marks on otherwise suspicious lesions, the system could have unanticipated and even deleterious effects on performance.²

Observational studies may be vulnerable to confounding, yet our results were not clearly explained by differences in the characteristics of patients, radiologists, or facilities. Nor were our findings attributable to outliers in the data. Although one facility used CAD for only 2 months, results were similar after excluding this facility. Finally, the sensitivities in our study are consistent with those in many previous community-based studies.³

Although some of the correspondents cite the inexperience of radiologists at facilities using CAD in our study, more than 70% of these radiologists had 10 or more years of mammography experience. Self-reported annual reading volumes among study radiologists (including those at facilities without CAD) may suggest that larger numbers of mammograms should have been available. But radiologists may interpret many mammograms outside study facilities.

The methods of the ROC analysis, including adjustment for reader characteristics, have been described elsewhere.⁴ The ROC curves are symmetric because the same standard deviation is assumed for the underlying latent distributions, an assumption that is supported by the fitted model and the symmetric shape of the empirical ROC distribution. The BI-RADS scale has six possible values (0 to 5), all of which were adequately represented in our large, population-based sample.

Feig et al. cite a significant increase in the rate of detection of DCIS in our study. However, the use of CAD was not associated with a significant increase in the rate of detection of either invasive breast cancer or DCIS. Rather, the proportion of total cancers detected that were DCIS increased with CAD (from 28.1% to 37.4%, $P=0.049$). Although the benefits of early DCIS detection are plausible, the benefits of CAD would be more certain if it clearly increased detection of invasive breast cancer. An adequately powered, randomized trial with this end point would require the interpretation of hundreds of thousands of mammograms by dozens of radiologists,⁵ and to our knowledge, no such study is planned. Thus, larger observational studies of the use of CAD by diverse radiologists are necessary to clarify the relative benefits and harms of a now widely disseminated technology.

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Weekend Admission for Myocardial Infarction

TO THE EDITOR: Kostis et al. (March 15 issue),¹ who report that mortality among patients admitted for acute myocardial infarction is higher on weekends than on weekdays, provide strong evidence that this finding may be due to a lack of

invasive cardiac services on weekends. However, if hospitals that lacked the ability to provide these services on weekends also tended to lack other important characteristics influencing mortality (e.g., the staffing of superior nurses or better cardiac

surgeons), then the apparent association of lower rates of invasive cardiac services on the weekends with higher mortality may be a spurious one. The authors should have provided a fixed-effects analysis (controlling for each hospital in their models). If the lack of invasive services on weekends truly leads to worse outcomes, such weekend differences in mortality should occur within hospitals. As reported, one cannot rule out the possibility that much of the observed weekend effect may be due to the admission of patients to worse hospitals on weekends as compared with weekdays. Establishing that the weekend effect persists after controlling for each hospital would have strengthened the case for changing current staffing patterns.

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1. Kostis WJ, Demissie K, Marcella SW, Shao Y-H, Wilson AC, Moreyra AE. Weekend versus weekday admission and mortality from myocardial infarction. *N Engl J Med* 2007;356:1099-109.

TO THE EDITOR: The article by Kostis et al. does not reflect the dramatic changes that have occurred in the treatment of myocardial infarction in New Jersey. The study focused on patients who were treated between 1987 and 2002. During this interval, few patients underwent immediate angioplasty for ST-elevation myocardial infarction, even at institutions that had such a capability. In 2002, New Jersey began to allow community hospitals to perform primary angioplasty for ST-elevation myocardial infarction. This change resulted in a major increase in the availability of immediate angioplasty. In addition, public reporting of so-called door-to-balloon times has fostered an intense focus on the timely treatment of ST-elevated myocardial infarction.

I suspect that if Kostis et al. extended their study to the present day, they would see a smaller gap between weekday and weekend outcomes and a much higher utilization of invasive procedures on the weekends. Patients with symptoms of myocardial infarction on weekends should be immediately taken to a facility capable of performing primary angioplasty so that they can receive optimal treatment at all times.

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TO THE EDITOR: Kostis et al. document increased mortality from myocardial infarction, persisting at 1 year, among patients presenting on weekends as compared with weekdays and suggest a causal association with reduced availability of invasive care on weekends. However, their data show that mortality at 365 days changed little during the 16-year period they studied, despite a major increase in the use of invasive procedures. For example, the weekday mortality from 1987 to 1990 was 23.7%, as compared with a weekend mortality of 23.9% from 1999 to 2002, despite an increase in the proportion of non-Q-wave myocardial infarctions from 20.5% to 51.0% during this time. Only 5953 of 42,076 patients (14%) underwent coronary-artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) on weekdays during the period from 1987 to 1990, whereas in the period from 1999 to 2002, the corresponding weekend figure was 6884 of 15,542 (44%). These data and the increased mortality with weekend admissions of patients with other conditions that do not all require invasive therapy¹ suggest that the increase in mortality may be due to the decreased weekend availability of cognitive skills and other hospital services rather than to fewer invasive procedures directly.

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1. Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001;345:663-8. [Erratum, *N Engl J Med* 2001;345:1580.]

TO THE EDITOR: Kostis et al. report that for patients with acute myocardial infarction, hospitalization on weekends, as compared with weekdays, is associated with increased mortality. A lower rate of performance of invasive procedures on weekends partly explains the difference. We analyzed mortality and invasive procedures on weekends and weekdays for hospitalizations for a first acute myocardial infarction, using the National Cause-of-Death, Swedish Myocardial Infarction, and Swedish Hospital Discharge registers.¹ The Swedish data confirm the increased mortality on weekends (Table 1). Revascularization procedures were performed more frequently on weekdays, as reported by Kostis et al. However, our data suggest that the difference in mortality can be explained only in

Table 1. Hazard Ratios for Death from Myocardial Infarction on Weekends, as Compared with Weekdays, in Sweden from 1968 to 2005, Adjusted for Age and Sex.

Interval between Admission and Death	1968–1979		1980–1989		1990–1999		2000–2005	
	Weekends (N=29,047)	Weekdays (N=93,569)	Weekends (N=50,973)	Weekdays (N=153,328)	Weekends (N=56,020)	Weekdays (N=161,038)	Weekends (N=35,022)	Weekdays (N=101,043)
	<i>hazard ratio (95% confidence interval)</i>							
2 Days	1.22 (1.17–1.27)		1.21 (1.17–1.25)		1.14 (1.10–1.19)		1.17 (1.10–1.23)	
7 Days	1.16 (1.12–1.20)		1.14 (1.12–1.17)		1.09 (1.06–1.12)		1.09 (1.05–1.14)	
30 Days	1.08 (1.05–1.10)		1.07 (1.05–1.09)		1.03 (1.01–1.06)		1.06 (1.02–1.09)	
365 Days	1.02 (1.00–1.04)		1.03 (1.01–1.04)		1.01 (1.00–1.03)		1.04 (1.02–1.07)	

part by differences in invasive procedures, since such a difference also existed during periods when PCI and CABG were not available. In addition, statistical adjustment for PCI and CABG during the 48 hours after acute myocardial infarction resulted in only a moderate decrease in the modeled difference in the period from 2000 through 2005 (hazard ratio for death at 2 days, 1.16; 95% confidence interval, 1.10 to 1.22). On the basis of autopsy records that were available from 1987, we found no difference between weekends and weekdays in rates of sudden death from acute myocardial infarction among patients who never reached the hospital.

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1. Hammar N, Nerbrand C, Ahlmark G, et al. Identification of cases of myocardial infarction: hospital discharge data and mortality data compared to myocardial infarction community registers. *Int J Epidemiol* 1991;20:114-20.

TO THE EDITOR: Although I draw qualitative conclusions that are similar to those of Kostis et al. in a study of data on national Medicare claims,¹ the mortality effects shown by Kostis et al. are much larger than those in the Medicare study (0.9% vs. 0.2% at 30 days) and raise concerns regarding unobserved patient heterogeneity.

Several commentators^{2,3} have suggested that higher weekend mortality⁴ may result from the delayed hospitalization of persons who had an onset of less severe symptoms on weekends. Al-

though the acute nature of myocardial infarction suggests little opportunity for elective deferral, the data indicate otherwise. Pooling all the years in Table 1 of the article by Kostis et al. shows that 26.5% of hospitalizations for myocardial infarction occurred on weekends, considerably less than the 28.6% that would have occurred if the incidence had been uniform. The authors observed higher rates of complications on weekends, which is consistent with the hypothesis that a reduced rate of weekend hospitalization leads to a weekday caseload of patients with more severe symptoms. Differences in observable measures of the severity of patients' symptoms suggest the presence of unobservable differences as well.

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4. Bell CM, Redelmeier DM. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001;345:663-8. [Erratum, *N Engl J Med* 2001;345:1580.]

THE AUTHORS REPLY: Silber notes that hospital-specific characteristics other than the ability to perform PCI may explain the difference in mortality between weekend and weekday admissions. The increased hazard ratio for 30-day mortality due to weekend admission was observed when the analysis was restricted to hospitals that could perform PCI (hazard ratio, 1.08) and when the availability of PCI was included in the Cox model (haz-

ard ratio, 1.04). Adjustment for individual hospitals, as suggested, yielded a similar result (hazard ratio, 1.04). These analyses also suggest that although the use of PCI is now more widespread, as noted by Altszuler, increases in the rate of PCI may not eliminate the difference in mortality between weekend and weekday admissions. In fact, we recently examined data from 2001 through 2004 (the latest available) and found a persistent difference in 30-day mortality for weekend admissions (12.1%) versus weekday admissions (11.4%) ($P=0.02$).

We agree with Fitzgerald that there may be differences in the breadth of expertise and the availability of certain medical therapies between weekdays and weekends. Nevertheless, the sequential Cox proportional-hazard models suggest that differential use of invasive cardiac procedures is one of a number of causes of the difference in mortality. Ljung et al., who also found higher mortality for weekend admissions, concur on this point.

Fitzgerald makes the excellent point that 1-year mortality did not change markedly in the 16-year period, whereas there was a substantial increase in the use of revascularization. We hypothesize that the reasons for the attenuation of the reduction in mortality at 1 year include the older age of patients in more recent years, the higher rate of coexisting illnesses, and possibly the discontinuation of beneficial pharmacologic therapies (e.g., angiotensin-converting-enzyme inhibitors, beta-blockers, and statins) after discharge.

As noted by Becker, we found that the highest proportion of patients with myocardial infarction were admitted on Monday (16.1%) and the lowest on Saturday (13.1%) and Sunday (13.4%). The higher rates of complications with weekend admissions may be attributable to more severe infarction, as Becker suggests, but could also be due to differences in management. In addition, the higher mortality for weekend admissions persisted after adjustment for complications as well as for demographic characteristics, coexisting illnesses, and the type and site of myocardial infarction. However, as noted, we could not control for unmeasured factors, including the time from symptom onset to admission. Further exploration of the factors underlying the difference in outcomes between weekend and weekday admissions may lead to the implementation of measures designed to mitigate the difference.

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Varicella–Zoster Vaccine

TO THE EDITOR: In their article about the varicella–zoster virus (VZV) vaccine for the prevention of herpes zoster, Kimberlin and Whitley (March 29 issue)¹ mention that the frequency and type of serious adverse events were similar for the vaccinees and placebo recipients. However, in the Adverse Event Monitoring Substudy, which involved a closely followed subgroup of 3345 recipients of the VZV vaccine (Zostavax, Merck) and 3271 placebo recipients, the rate of serious adverse events was higher among the vaccine recipients than among the placebo recipients (1.9% vs. 1.3%; relative risk, 1.53; 95% confidence interval, 1.04 to 2.25).² To assess further the rates of serious adverse events after vaccination with Zostavax, Merck has agreed to

conduct a postlicensure randomized, placebo-controlled clinical trial involving 6000 vaccine recipients and 6000 placebo recipients.³

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