morbidity and mortality in acute coronary syndromes and is effective antiangina therapy, superior to medication alone. However, the use of elective PCI in patients with stable CAD has not been shown to reduce future coronary events or mortality. Previous studies have shown that PCI of occluded “culprit” vessels after MI does not alter future cardiac/mortality outcomes, and preoperative PCI does not change the risk for surgery or perioperative cardiovascular complications. Now, this large study shows that elective PCI does not reduce future cardiac events or death in a large group of patients with multivessel disease and high event rates. Two important points can be made. First, in patients with stable angina, this study lends support to a “conservative” medical management approach first, using the many medications that are known to reduce cardiac events and mortality, such as aspirin, beta-blockers, and statins. Cardiac catheterization (with possible PCI) can be reserved for patients who have progressive, limiting angina despite medical therapy, since the benefit of PCI in these patients would be to reduce angina, not to prevent MI and death. In other words, there is little downside to waiting, and this more conservative strategy may save money by preventing unnecessary catheterization procedures. Second, in patients who have undergone cardiac catheterization in nonacute situations, either for diagnostic purposes or to assess severity of disease, PCI can be reserved for patients who fail medical therapy. Such an approach would reduce costs and complications from the procedure and the medical therapy (clopidogrel) required after the procedure.

RELATED REFERENCE

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TYPE 2 DIABETES MELLITUS

Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes
Nissen SE, Wolski K.

AIM
To determine whether the use of rosiglitazone in type 2 diabetes mellitus has an effect on cardiovascular outcomes.

METHODS
The authors pooled data from all placebo-controlled studies using rosiglitazone that lasted more than 6 months and reported cardiovascular outcomes. More than 40 studies were found, including published peer-reviewed articles, FDA website data, and pharmaceutical company files. Studies were excluded if there were zero events. Data were analyzed for risk for MI or cardiovascular death.

RESULTS
Over 27,000 subjects were included in the data set. MI was 43% more common in patients on rosiglitazone (RR, 1.43 [CI, 3-97]), and cardiovascular deaths were 64% more common, although this latter difference approached, but did not meet, statistical significance (RR, 1.64 [CI, -2 to – 197]). Overall event rates were low; only 0.5% of study participants had cardiovascular events, and mean follow-up was less than 1 year.

CONCLUSIONS
Rosiglitazone may increase risk for MI in patients with type 2 diabetes mellitus. However, the inherent limitations in this and all meta-analyses make firm conclusions based on this article impossible.

IMPLICATIONS FOR INTERNAL MEDICINE
This article received much attention in the media, portrayed as an example of a flaw in the FDA approval process for new medications. Rosiglitazone had become the leading branded medication for treatment of type 2 diabetes mellitus. Like the closely related thiazolidinedione (TZD) pioglitazone, it improves glycemic control, lowering glycosylated hemoglobin about 1-1.5%. However, previous studies have demonstrated and increased risk in congestive heart failure for both of these agents, in addition to weight gain and edema, and no studies to date shown improvements in microvascular and macrovascular “hard” outcomes. Since this particular article was released, there have been several articles reporting similar concerning findings. However, not all studies have reached this same conclusion. RECORD is an ongoing study designed to compare rosiglitazone to other oral agents as second “add-on” oral agents in diabetes. As a result of the publicity surrounding the NEJM report, an interim analysis was performed and published, showing no significant increase in coronary events or death in patients on rosiglitazone. Thus, it is still not possible to draw firm conclusions, although there are certainly concerns raised about the safety of
this agent. Alternatively, a similar meta-analysis was performed on available data using pioglitazone, and in 19 studies involving over 16,000 patients, pioglitazone reduced cardiovascular outcomes (hazard ratio, 0.82 [CI, 0.7-0.94]).

At this time, a definitive study has not yet been done. It is still reasonable to use TZDs in type 2 diabetic patients in whom other agents, that have a clearer safety record, have failed, such as metformin and sulfonylureas. If a TZD is used, pioglitazone is the preferred agent: It is has a favorable effect on lipids, compared with the slightly unfavorable effects seen with rosiglitazone, and no data suggested that pioglitazone increases cardiovascular risk. On the contrary, pioglitazone may reduce cardiovascular risk.

This study and the others that came after it, highlight the problems with using surrigeate markers in diabetes. Improvement in glycemic control, while desirable in theory, may not translate to improved outcomes. Future agents for diabetes should be scrutinized more carefully and not promoted for use without better outcome data over the long-term.

RELATED REFERENCES

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ASTHMA

Randomized comparison of strategies for reducing treatment in mild persistent asthma

The American Lung Association Asthma Clinical Research Centers.


AIM
To determine whether patients with mild persistent asthma that is well controlled by twice-daily inhaled corticosteroids can be managed with simpler treatment regimens.

METHODS
After receiving 6 weeks of twice-daily inhaled fluticasone, 500 patients with well-controlled, mild persistent asthma were randomly assigned to one of three treatment arms: 1) continued twice-daily inhaled fluticasone; 2) once-daily inhaled fluticasone plus salmeterol; or 3) once-daily oral montelukast. Outcomes focused on “treatment failure”, which included such metrics as the need for more intense management and physiologic deterioration and measurement of symptom scores, after 6 months.

RESULTS
Applying this broad definition of treatment failure, the authors found similar failure rates for patients continued on twice-daily inhaled fluticasone or managed with once-daily inhaled fluticasone plus salmeterol (20.2% and 26.4%, respectively) as well as a higher failure rate (30.3%) for patients treated with once-daily oral montelukast (hazard ratio, 1.6 [95% CI, 1.1 to 2.6]). The percentage of days during which patients were symptom free was similar across all three treatment groups (5.8%, 82.7%, and 78.7% [P > 0.10 for all comparisons]). By the end of the study, more patients assigned to receive twice-daily fluticasone (69.7%) or once-daily fluticasone plus salmeterol (78.4%) wished to continue their assigned treatment regiment, compared with those assigned to receive montelukast (56.4%) (P < 0.001).

CONCLUSIONS
Patients with mild persistent asthma that is well controlled with twice-daily fluticasone can be changed to once-daily fluticasone plus salmeterol. Once-daily montelukast proved to be inferior by the outcomes measures in this study but may be an acceptable regimen for some patients.

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KIDNEY STONES

A systematic review of medical therapy to facilitate passage of ureteral calculi
Singh A, Alter HJ, Littlepage A.