We selected miR-1 for functional analysis in mesothelioma because we have ongoing interests in this microRNA. We discussed this topic in the Results and Discussion sections of our study. We agree that other miR-1 family members and multiple other microRNAs identified from our list of most differentially expressed microRNAs are interesting, too. Further studies elucidating distinguished functions of other microRNAs are being conducted.

Polymerase chain reaction (PCR) analysis of known apoptotic genes was done to confirm the apoptotic phenotype of transfected cell lines. Correlation analysis of miR-1 and its gene targets is not highly useful, since specific functional information of those interactions cannot be discerned. Identifying and confirming microRNA direct gene targets were not in the scope of our investigation and were never the goal of this study.

In our experimental procedures, we described in great detail which company’s RNA products were used for microRNA overexpression, the transfection reagents used, the system used to run our real-time PCR, and the list of gene primer sequences used to perform PCR or the catalog number of the microRNA assay. We followed recommendations of the manufacturer where indicated. We searched PubMed, and as of August 15, 2013, many of the microRNAs we mentioned as examples of putative, novel mesothelioma-associated microRNAs remained consistent. In the Discussion section, we limited the context to prior microRNA profiling studies, not an encyclopedic review of every microRNA that has heretofore been mentioned with mesothelioma. The Kubo et al article is not a microarray profiling study, but details the methylation status of miR-34b and its functional implication.

In summary, we have identified a set of underexpressed and overexpressed microRNAs specific to mesothelioma based on a survey of human tissue specimens. We reported that overexpression of miR-1 in mesothelioma cell lines induces apoptosis. We welcome subsequent independent studies of miR-1 in mesothelioma. We anticipate the other microRNAs we have identified will contribute to ongoing research in mesothelioma.

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Response

To the Editor:

We thank Dr Hunasikatti for his comments regarding our article on the management of patients with suspected OSA in the postoperative period.1 Although we agree that all institutions should have established protocols for patients with OSA in the postoperative period2 and that positive airway pressure plays a role in preventing postoperative complications, he makes some assertions that we believe are unsupported.

Our study specifically addressed patients without OSA presenting before surgery. We used screening to identify those at high risk for OSA; they could not have been on CPAP for the past several months. Furthermore, Dr Hunasikatti states that autotitrating positive airway pressure (APAP) therapy was a poor selection for therapy because positive airway pressure (PAP) takes 1 to 3 months to show clinical benefit, which is incorrect. The most pressing concern for the postoperative patient with OSA is preservation of airway patency and ventilation. During the first night of PAP titration, airway patency is restored, and ventilation resumes very quickly. It takes minutes. Additionally, although improving sleepiness and psychomotor performance was not a goal of the study, CPAP significantly improves sleepiness after only 1 day and significantly improves simulated driving performance after only 2 to 7 days of treatment.3 Thus, we believe it reasonable that APAP could acutely improve airway patency and potentially reduce delirium.

Dr Hunasikatti also suggested that using bilevel PAP would have been a better choice in part because “many patients” tolerate bilevel PAP better than CPAP. The literature indicates no significant difference in control of OSA, mask discomfort, adverse nasal symptoms, or treatment adherence.4 Additionally, when a decision is made to empirically treat suspected OSA, one must either guess the pressure, use an algorithm to determine pressure,6 or use APAP to provide therapy, and overtitrated bilevel PAP can provoke central apnea. We chose APAP because of abundant evidence that these devices often provide similar efficacy when treating OSA in the outpatient environment.9

The use of APAP as empirical treatment of patients with suspected OSA in the hospital practice setting is common. The data showed that APAP (incompletely) reduced sleep-related respiratory events, but we did not see a significant reduction in complications. We agree that this could be partly due to an underpowered study. However, we assert that addressing this important safety issue will likely require more than just PAP and instead will require better risk stratification plus intensified monitoring of those at highest risk. Finding this population and determining its needs is an important next step.

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REFERENCES
