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THE AUTHORS REPLY: We agree with Finucane that it is important to monitor and treat hyponatremia after a ruptured cerebral aneurysm. He cites a study that showed fewer instances of hyponatremia among patients with spontaneous subarachnoid hemorrhage who were treated conservatively than among those who were treated with clipping or coiling.[1] The group treated conservatively, however, consisted mostly of patients with subarachnoid hemorrhage in which an aneurysm could not be detected. The natural history of nonaneurysmal subarachnoid hemorrhage usually differs from that of aneurysmal subarachnoid hemorrhage. Hyponatremia is infrequently the cause of significant impairment or death in patients with subarachnoid hemorrhage. For example, one recent multicenter review showed that hyponatremia had no bearing on the outcome 3 months after subarachnoid hemorrhage.[2]

Torres et al. share their algorithm for screening patients with autosomal dominant polycystic kidney disease. Although the incidence of cerebral aneurysms in the population with this disease is generally thought to be higher than that in the population without this disease, estimates of the prevalence have varied considerably. On the basis of currently available data, the screening approach outlined by Torres and colleagues appears to be reasonable.

Whiteley and Al-Shahi point out the importance of the World Federation of Neurosurgical Societies Scale for subarachnoid hemorrhage. More than 30 clinical grading scales for subarachnoid hemorrhage have been described. The most commonly used scales are the World Federation of Neurosurgical Societies Scale and the Hunt and Hess Scale. Both have reasonable interobserver reliability and correlate well with the ultimate clinical outcome.[3] Despite the recommendations of the World Federation of Neurological Surgeons to use their scale as a universal scale, most neurosurgeons still prefer the Hunt and Hess Scale; in a review of articles on subarachnoid hemorrhage that were published between 1985 and 1992, 71% of reported studies used the Hunt and Hess Scale, whereas only 19% used the World Federation of Neurosurgical Societies Scale.[4]

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Use of Statins and Outcome of BCG Treatment for Bladder Cancer

TO THE EDITOR: The intravesical administration of bacille Calmette–Guérin (BCG) vaccine for high-risk, non–muscle-invasive bladder cancer and carcinoma in situ is one of the most successful immunotherapies to date.[1] Studies in animals have shown that the generation of effector cells, called BCG-activated killer cells, depends on type 1 helper T (Th1)–type cytokines.[2] In humans, a high Th1-biased urinary cytokine profile after several weekly intravesical instillations of BCG correlates with a better clinical response.[3]

Statins have cholesterol-lowering properties and also immunomodulating actions. Several reports have indicated that statins can induce

Table 1. Baseline Characteristics of the Patients.

Characteristic	All Patients (N=84)	Patients Taking Statins (N=19)	Patients Not Taking Statins (N=65)	P Value	Odds Ratio (95% CI)
Age at diagnosis — yr				0.44	
Median	65	70	63		
Interquartile range	61–70	58–74	60–70		
Sex — no. (%)				1.00	
Male	77 (92)	18 (95)	59 (91)		
Female	7 (8)	1 (5)	6 (9)		
Total cholesterol — mg/dl				0.50	
Median	202	192	203		
Interquartile range	191–213	161–221	191–213		
Median follow-up — mo	46	37	50	0.20	
Mean no. of recurrences					
First year	0.4	0.5	0.4	0.40	
Total	0.9	1.2	0.8	0.20	
Progression — no. (%)	22 (26)	10 (53)	12 (18)	0.004	4.9 (1.64–14.69)
Cystectomy — no. (%)	17 (20)	8 (42)	9 (14)	0.01	4.5 (1.43–14.30)

antiinflammatory type 2 helper T (Th2)–type cytokines (interleukin-4, interleukin-5, and interleukin-10) and inhibit the secretion of interleukin-2, interleukin-12, interferon gamma, and tumor necrosis factor through the inhibition of signal transducer and activator of transcription 4 (STAT4) and the transcription factor T-bet. The result is strong attenuation of the Th1-type immune response and promotion of the development of Th2 cells.[4,5]

We retrospectively analyzed the clinical outcomes for 84 patients who had received BCG immunotherapy for the treatment of non–muscle-invasive bladder cancer; 19 of the patients had taken statins during BCG immunotherapy, and 65 had not (Table 1). We determined the number of recurrences during the first year, the number of total recurrences, tumor progression, the time to cystectomy, and the time to the development of distant metastases. The two groups had similar medical histories, follow-up times, and pathological features.

The median follow-up was 46 months. The number of recurrences during the first year or subsequent years did not differ significantly between the groups. However, in 53% of the patients who took statins, the tumor became more aggressive, whereas this change occurred in only 18% of the patients who did not take statins (P=0.004; odds ratio, 4.9; 95% confidence interval [CI], 1.64 to 14.69). Similarly, 42% of the patients in the statin group had to undergo radical cystectomy, as compared with only 14% of the patients who did not take statins (P=0.01; odds ratio, 4.5; 95% CI, 1.43 to 14.30). Among the patients who underwent radical cystectomy, the number in whom metastases developed and the time to their development were similar in the two groups.

Our observations suggest that the discontinuation of statin therapy during BCG immunotherapy might improve the clinical outcome, since the use of statins was significantly associated with an increased risk of tumor progression and a subsequent need for radical cystectomy.

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