Letter to the Editor

Attributable Risk Calculations for Testicular Microlithiasis

I read with interest the study by Heller et al,[1] "Testicular Microlithiasis: Prevalence and Association with Primary Testicular Neoplasm." The problem of testicular microlithiasis has vexed radiologists and urologists for decades, and the authors are to be commended on their thoroughly documented and large cross-sectional study. It remains unclear whether microlithiasis is itself a risk factor for testicular carcinoma or merely a marker for some other, as yet unknown, risk factor or exposure. In a cross-sectional study, a causal–temporal sequence cannot be formally inferred. However, if the sequence is presumed and microlithiasis is directly treated as a risk factor for testicular cancer, the data are subject to additional epidemiologic analysis that may be of interest to your readers.

As the authors enumerate in their Table 1, the prevalence of testicular cancer was 11.6% in men with microlithiasis, 1.5% in men without microlithiasis, and 2.3% in the total study population. The relative risk of testicular cancer is thus 7.67 times higher in men with microlithiasis than it is in other men. How much of this additional risk is actually attributable to the presence of microlithiasis? The answer to this question takes into account the overall prevalence of the risk factor in the population and provides insight into the true effect of the risk factor on the disease in the population—the consideration that should drive policy recommendations.

Among men with microlithiasis, the excessive occurrence of testicular cancer is simply the difference between the risk in men with microlithiasis (116 cases per 1,000 men) and the risk in other men (15 cases per 1,000 men) (Table 1). Thus, the attributable risk is 101 per 1,000 cases, meaning that in 1,000 men with microlithiasis, 101 testicular cancers could be prevented (or detected earlier) if it were possible to eliminate the risk factor of microlithiasis (or to perform dedicated surveillance for those who have it). In fact, among men with microlithiasis, the attributable risk percentage is 87.0%, meaning that 87.0% of testicular cancers in these men are actually related to their microlithiasis.

How does this play out in the population as a whole? The prevalence of microlithiasis in the study population was 7.67%. Population-attributable risk is the product of the attributable risk in the exposed population and the prevalence of that exposure in the total population. Thus, the population-attributable risk is 8 per 1,000 cases, meaning that in the total population, eight cases of testicular cancer per 1,000 men could be attributed to microlithiasis, constituting 33.6% of all testicular cancer in the population. The population-attributable risk percentage of 33.6% means that 33.6% of testicular cancer is associated with microlithiasis and could potentially be prevented or its disease course altered by modification of this risk factor.

Thus, a full one-third of testicular cancer was attributable to microlithiasis in this study. The authors note that their population is subject to a selection bias because sonographic examinations were only being performed in patients with masses or other symptoms. This would tend to overestimate the prevalence of both cancer and microlithiasis and may limit the generalizability of these findings. Furthermore, as noted above, the attributable-risk analysis presumes a causal–temporal sequence that cannot be derived directly from cross-sectional data, and this must be considered an additional limitation. Generally, discussions of attributable risk are based on incidence data (as can be derived from a cohort study) rather than prevalence data, as in this cross-sectional study. As such, calculations of attributable risk are subject to bias associated with method of sampling, and conclusions are valid only within the population context of men undergoing scrotal ultrasound.

Over the years, there has been little consensus on the management of microlithiasis, and

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TABLE 1
Attributable-Risk Calculations for Microlithiasis as a Risk Factor for Testicular Cancer in 6,002 Patients

	Attributable Risk		Attributable Risk Percentage	
	Definition	Value	Definition	Value
Men with microlithiasis	Disease rate among those exposed to risk factor less disease rate in unexposed	101 cases per 1,000 men	Attributable risk divided by disease rate in exposed group × 100	87.0%
Population as a whole	Disease rate in total population less disease rate in unexposed	8 cases per 1,000 men	Population-attributable risk divided by disease rate in total population × 100	33.6%

recommendations have covered the spectrum from no follow-up through testicular self-examination,[2] serial ultrasounds,[3] and even testicular biopsy.[4] When viewed through the lens of attributable risk, the data in the study by Heller et al lend support to the idea of testicular microlithiasis as a true, although unfortunately nonmodifiable, risk factor for testicular cancer. Current science does not enable us to prevent these cancers. However, this analysis underscores the need for standardized recommendations for clinical and imaging follow-up in patients with microlithiasis, with the goal of detecting cancer earlier and minimizing associated morbidity and mortality.

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